

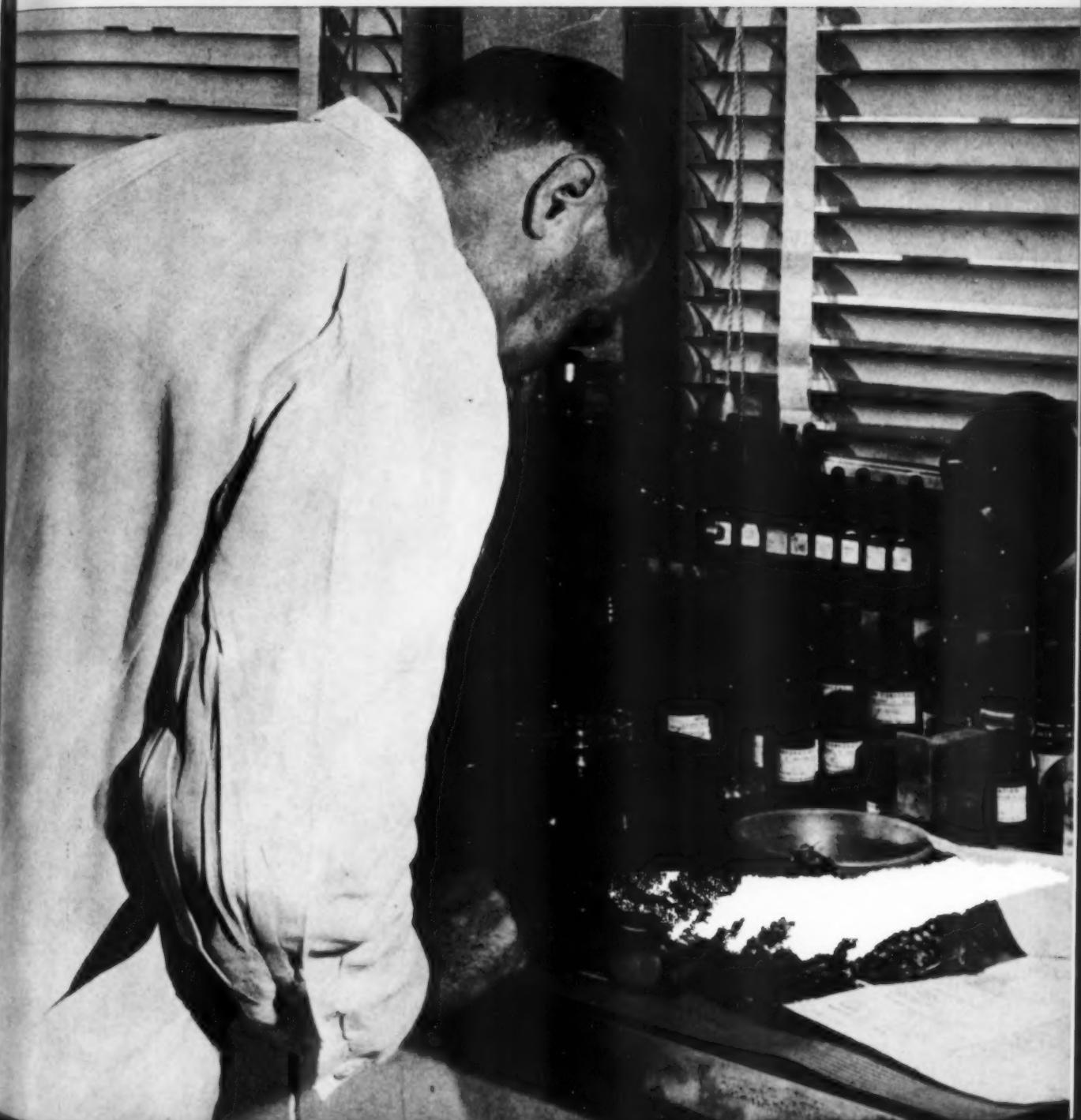
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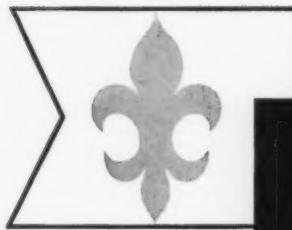
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American Perfumer

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Propiedades clave de almidones para aplicaciones farmacéuticas y de cosméticos

Un cambio en una de las propiedades inter-relacionadas del almidón puede producir cambios en otras propiedades acompañantes. Se ha extendido la selección de las propiedades que se deseen por la investigación de productos. Esto está dando a los formuladores de cosméticos nuevos materiales con los cuales trabajar.

Die wesentlichen Eigenschaften der Stärken bei kosmetischer und pharmazeutischer Anwendung

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Panax Ginseng in cosmetic formulations? . . . by Dr. W. A. Meer and George Meer, Jr. 29

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Le "Panax Ginseng" et les formules cosmétiques?

Les Orientaux l'ont employé pendant des années en tant que produit tonique et produit de rajeunissement. Malgré bien d'autres propriétés, ce dernier à récemment soulevé un certain intérêt pour son emploi avec les cosmétiques.



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"Panax Ginseng" en formulaciones de cosméticos?

Los orientales lo han usado por muchos años como tónico y rejuvenecedor. Estas, además de otras propiedades han despertado interés últimamente para su uso en formulaciones de cosméticos.

Panax Ginseng in kosmetischen Formulierungen?

Die Orientalen wenden es seit Jahren als Stärkungs- und Verjüngungsmittel an. Diese und andere Eigenschaften haben in neuerer Zeit das Interesse für die Anwendung in kosmetischen Präparaten erweckt.

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De récentes restrictions gouvernementales quant à l'emploi de ce produit dans les cosmétiques amène cette question. La discussion et les offres de l'auteur sont extrêmement opportunes.

Es la bergamota un sensibilizador?

Restricciones gubernamentales recientes sobre el uso de este producto en cosméticos dan nacimiento a esta pregunta. Las discusiones y proposiciones del autor son muy oportunas.

Ist Bergamot ein Sensibilisator?

Kürzlich von der Regierung erlassene Beschränkungen bezüglich des Gebrauchs dieses Erzeugnisses in kosmetischen Mitteln lassen diese Frage auftreten. Die Besprechung und Vorschläge des Authors sind ausserordentlich zeitgemäß.

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Un cours pratique pour l'éducation professionnelle des parfumeurs

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Systèmes de suspension

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Sistemas de Suspensión

Se discuten varias suspensiones ya que pertenecen a varias clases de preparaciones. El autor cita controles primarios básicos.

Suspensions-Systeme

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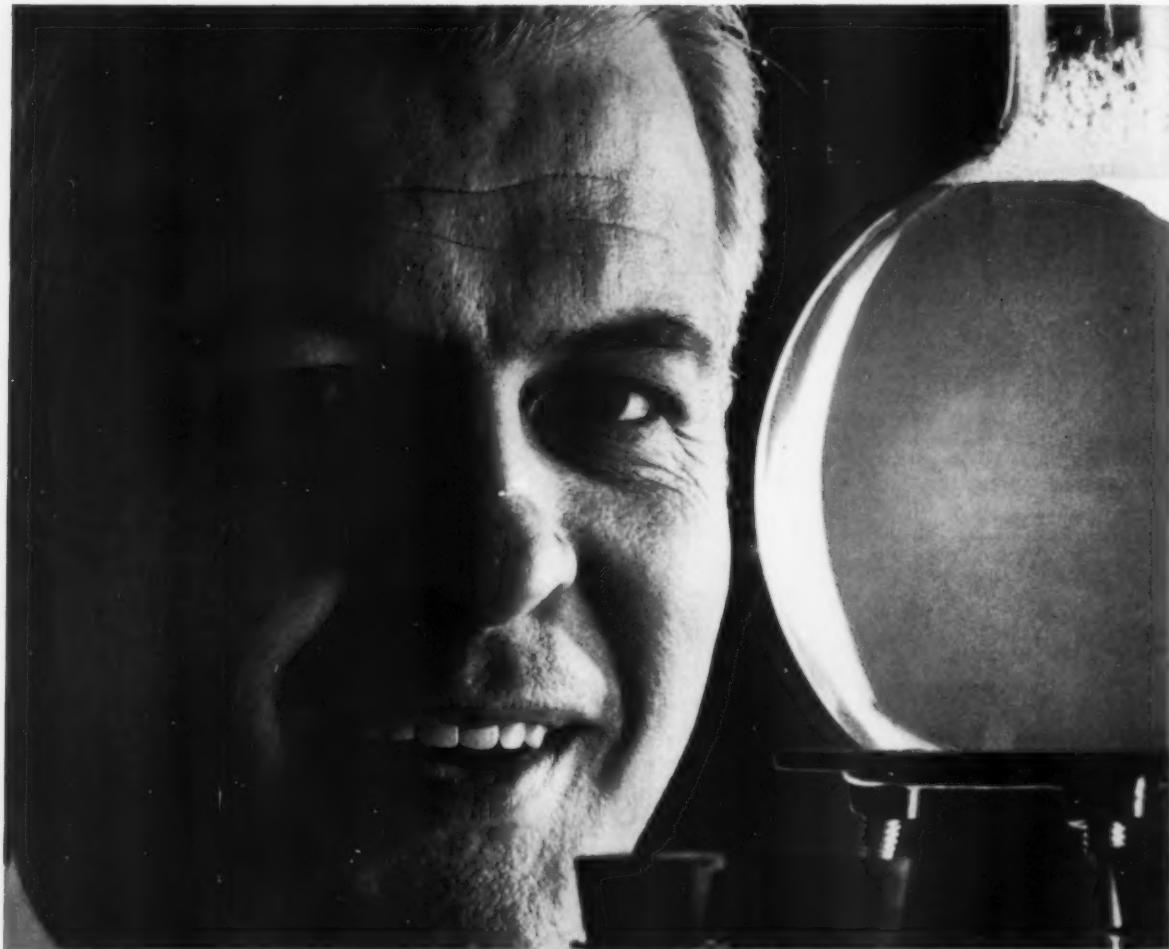
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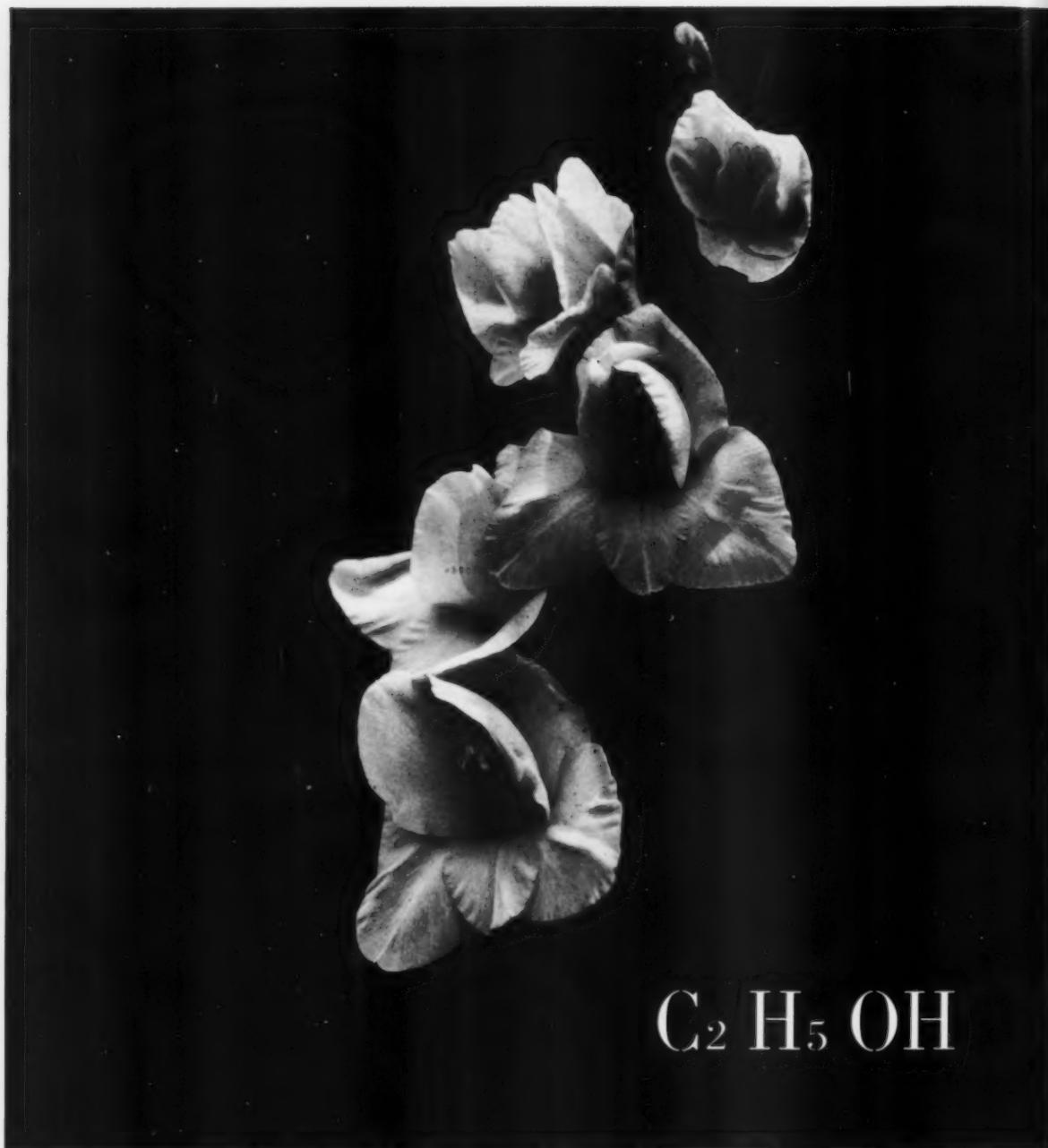
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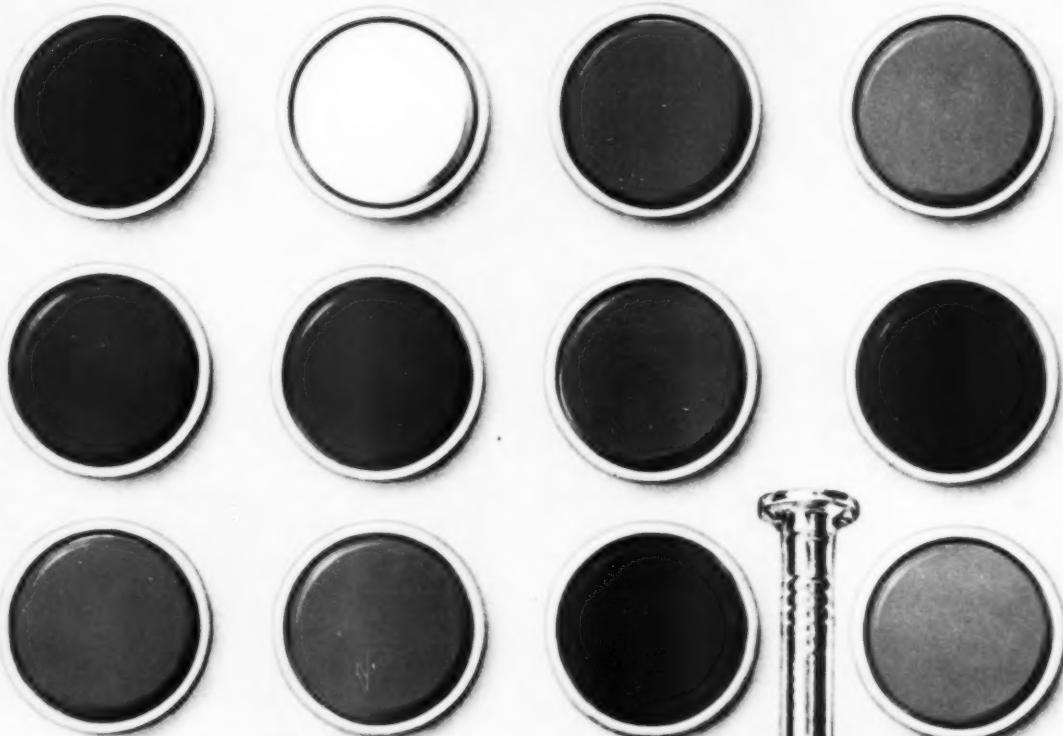
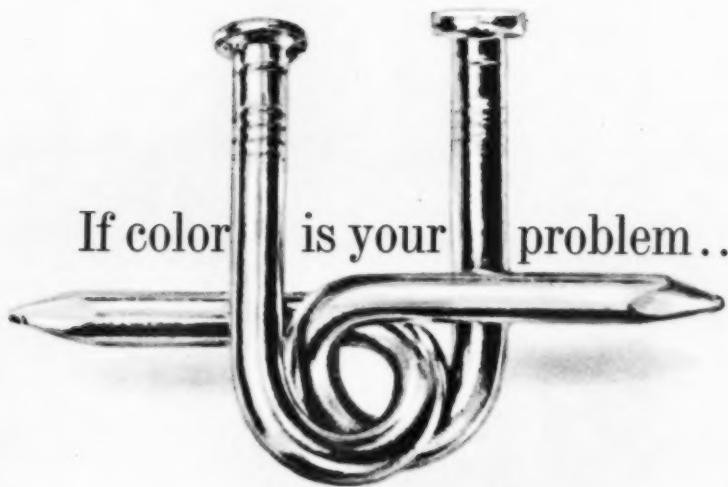
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REACTIONS

Odor and Molecular Constitution—a postscript

BY M. G. J. BEETS, Director, Research and Development
International Flavors & Fragrances, Hilversum, Holland

After the publication of my paper "Odor and molecular constitution" in the June issue of the AMERICAN PERFUMER, page 54, I received a number of letters which show that some aspects of my concise survey of the P.F.G. concept require some additional explanation.

In the first place I wish to stress again the point that the P.F.G. concept does not pretend to present a complete theory of the mechanism of olfaction.

The series of events which lead to the observation of an odor sensation consists at least of the following stages.

1. Transport of the odorant molecules.
2. Interaction between many molecules with many sites of the receptor surface.
3. Formation of the stimulus.
4. Transport of the stimulus.
5. Formation of the odor sensation.
6. Observation, i.e. verbal expression or electrical response.

Concurrent phenomena are the removal of odorant molecules from

the receptor surface by inhaled air and restoration of the original structural conditions of the receptor surface.

The steps 3, 4 and 5 can be assumed to be true transporter translation steps. In other words, these steps transport the results of the interaction to other parts of the organism or they translate them into entirely different forms. But every structural detail of the original interaction result is represented by some structural detail of the odor sensation.

Consequently, we may assume that the interaction and the sensation are perfectly correlated and the sensation is a function of both the structure of the stimulant molecule and the structure of the receptor.

The P.F.G. concept accepts the fact that we do not know the mechanism of the interaction. It attempts to construct a model of the contribution of the odorant molecule to the interaction process and to correlate the predictable consequences of this contribution with the observed odor sensation.

This means that the P. F. G. concept excludes the, as yet, unknown contribution of the structure of the receptor to the interaction.

We may hope that, as our insight in this matter increases, a P.F.G.R. (Profile-Functional-Group-Receptor) concept will be proposed to complete the picture and to fill up the obvious gaps in our understanding which the P.F.G. concept cannot explain.

A further characteristic of the P.F.G. concept is, that it treats olfaction as a statistical phenomenon.

One molecule interacts with one site of the receptor surface and the resulting single quantum of information is transported and translated before it contributes to the observed sensation. The latter is the total of a very large number of such quanta.

The statistical composition of the population of molecular contributions to the odor sensation may be anything between perfect homogeneity (which can only occur when a number of identical molecules interact in the same way with identical receptor sites) and complete chaos. Deviations from perfect homogeneity of the population can have several origins.

a. Action of a mixture of non-identical molecules on either identical or non-identical receptor sites. This case is ignored

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since only stimulation with pure materials is considered.

b. Action, identical or non-identical, of identical molecules on non-identical receptor sites. Since we know very little about the structure of the receptors this type complicates our picture to an unknown extent.

c. Non-identical actions of identical molecules on identical sites.

The scope of the P.F.G. concept is consciously limited to the latter type and variations of the receptor type are necessarily ignored because our knowledge is insufficient to include them in our considerations. However, the deviation from reality obtained in this way may be within reasonable limits since the possibility exists that mainly one type of receptor responds to the interaction with a number of identical molecules.

According to the P.F.G. concept we assume that variations of the interaction with molecules of one type are caused by variations of the orientation in which they are absorbed.

The nature and the sterical environs of the functional group determine the absorption affinity and the orientation spectrum of the absorbed molecules on the receptor surface. Consequently, they influence both the intensity and the nature of the odor.

A functional group causing a high absorption affinity can be expected to increase the number of molecules absorbed, the average time of absorption, and the uniformity of the orientation pattern (high, narrow Gauss curve). In terms of odor sensation this means

high odor intensity, rapid fatigue and a characteristic, clearly recognizable odor type.

When no functional group is present, e.g. in saturated hydrocarbons, the absorption affinity will be low. The fraction of molecules abstracted from the air by absorption and their average time of absorption will be small and the orientation pattern will be random (flat, wide Gauss curve). The odor can be expected to be weak and uncharacteristic.

Some of my correspondents have understood that the P.F.G. concept requires saturated hydrocarbons to be odorless. This is not true. Also a molecule without a functional group is absorbed under proper conditions but since there are (except for sterical reasons) no preferential orientations, the average profile and consequently also the resulting odor sensation are blurred.

The presence of more than one functional group, except when they are in neighboring positions can be expected to decrease the homogeneity of the orientation pattern to an extent, depending on the nature and sterical environs of each group. The carbonyl group seems to be the strongest orientation determining factor and its influence may be expected to dominate largely the orientation pattern of any type of molecules in which it is present.

According to the P.F.G. concept, the profile of the absorbed molecule determines the nature of the odor sensation. In this connection, the molecular profile should be considered from the vectorial point of view. A sheet of paper looks

like a square from one direction and like a straight line from another.

The contribution of the molecular profile to the interaction process in one orientation is, except when the molecule is a sphere, entirely different from that in another.

This means that the molecular contributions to the odor type of a number of identical molecules with a partly disorganized orientation pattern may vary widely since identical molecules absorbed in different orientations have different effective profiles. However, it seems very probable that the specific structures of the receptors have a selective function and that out of the population of effective profiles in a pattern, only part leads to a positive response in the interaction process.

A molecule of the type P_1FP_2 , in which F represents a functional group attached to two profile groups P_1 and P_2 , may contribute to the odor picture in two different types of orientations, each of which perhaps becomes effective by absorption at a specific receptor type. In the first, the profile group P_1 dominates while P_2 is ineffective; in the second, the situation is reversed. In the odor character of compounds of this structural class, two different notes may be represented and, in favorable cases, recognizable.

Dr. F. Exner (recently from Germany) has been kind enough to draw my attention to an interesting example of this case: isomyl phenylacetate in the odor of which the honey note (character-

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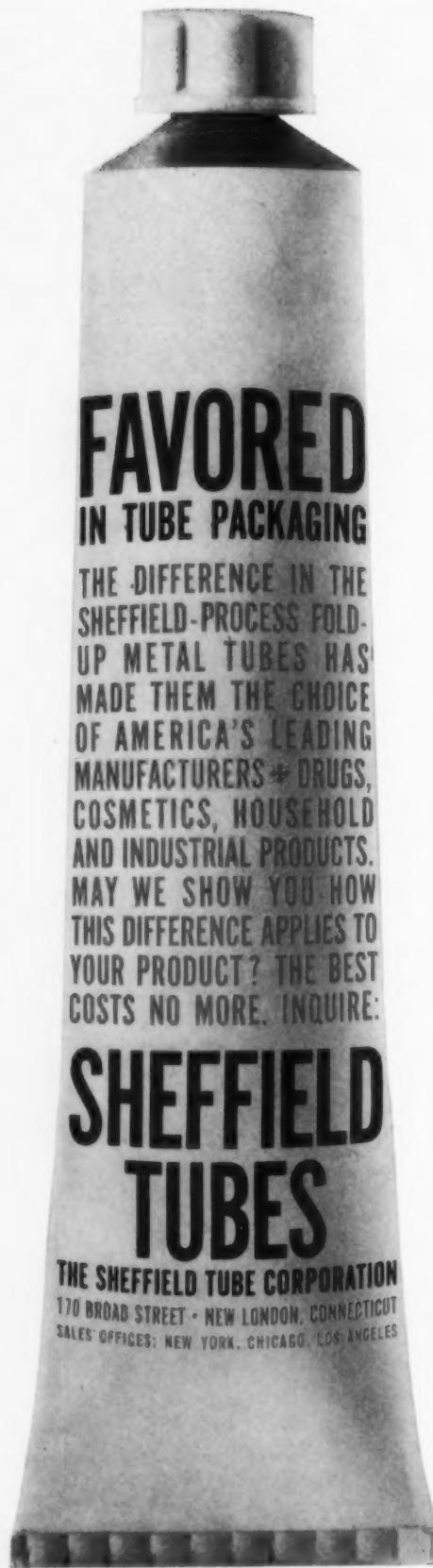
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istic for the phenylacetic acid profile) and the remotely chocolate like note, (characteristic for the isoamyl group) can be distinguished.

I hope that these additional explanations may contribute to a better understanding of the P.F.G. concept and of its obvious limitations.

Hair stick

In looking over back issues of the AMERICAN PERFUMER we found a formula for a hair stick by the Fanning Chemical Corporation that we would like to try. Would you please send the address of this company? We would also like a source of supply for plastic containers for a hair stick.—J. E., North Carolina.

The former address of the Fanning Chemical Corporation is 573 Ferry Street, Newark 5, New Jersey. We believe the company has changed ownership recently. We have not seen any hair sticks in plastic packages, but metal containers have been used by a number of companies. One of the producers of these metal containers is the Clark Manufacturing Co., Rockford, Illinois.

Wants materials

We are interested in purchasing Nonanediol, or Nonylendiol and Myrcene, and would be grateful if you would advise the name and address of a manufacturer in the United States.—E. L., Great Britain

Myrcene is supplied by The Glidden Co., Organic Chemical Division, P. O. Box 389, Jacksonville, Florida; Nonanediol Acetate is obtainable from Givaudan-Delawanna, Inc., 321 West 44th Street, New York 36. Small experimental quantities of Nonanediol may be had from International Flavors and Fragrances, Inc., 521 West 57th Street, New York 19. We are unable to supply any information regarding Nonylendiol. Perhaps readers can help us out?

Notice

The abstracts which appeared on pages 42 and 43 of the Sept. issue were of papers presented before the Industrial Pharmacy Section and the Section on Practical Pharmacy at American Pharmaceutical Association Convention, April 23-28, 1961.

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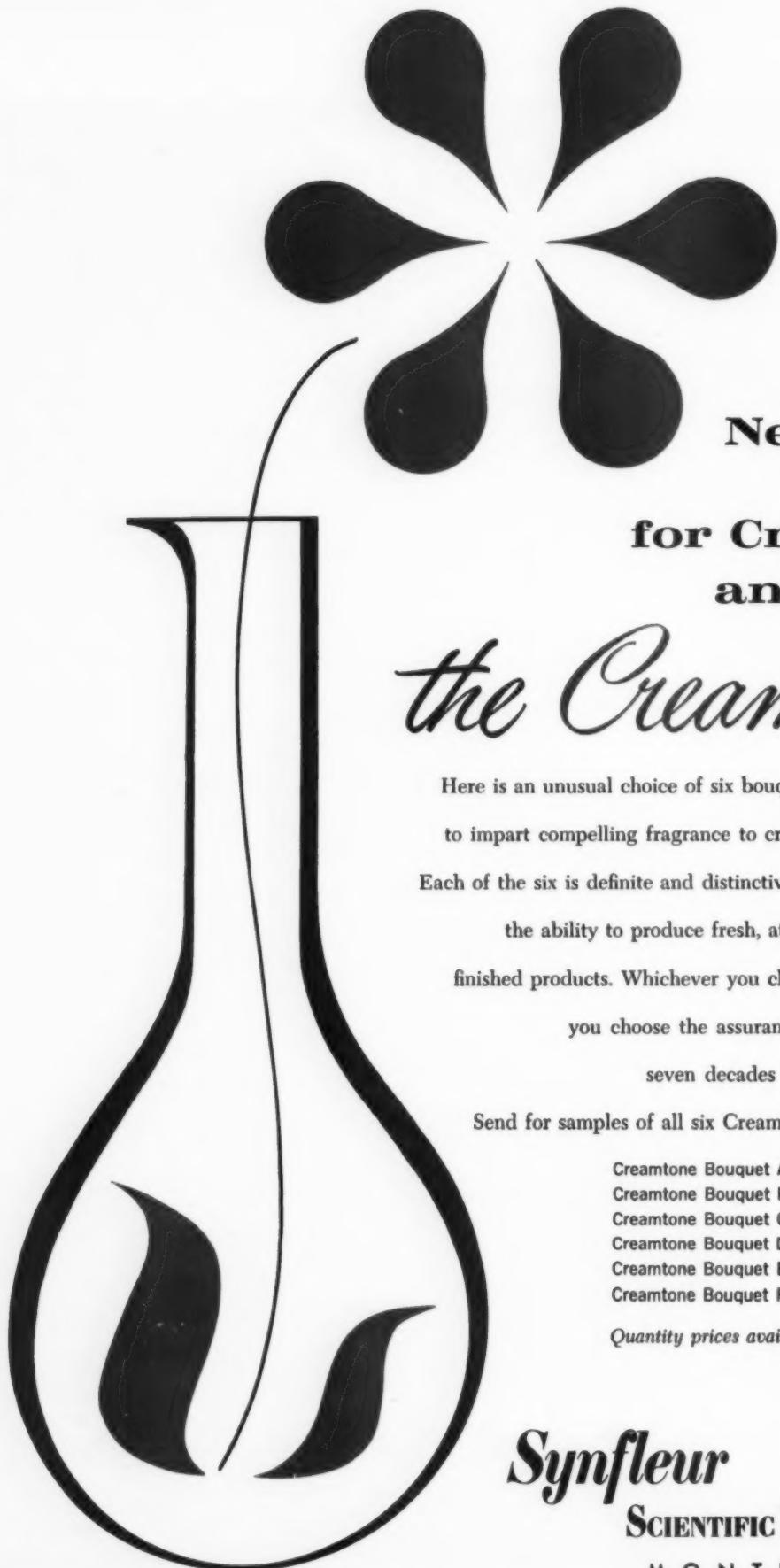
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Notes From Abroad

My wife and I again had the opportunity to see old friends abroad during our trip of twenty-five days, coinciding with the Council Meeting of the I.F.S.C.C. in Copenhagen.

New officers of the I.F.S.C.C. are Dr. Ludwig Masch, president and Gui Dony, treasurer; Comité de Direction, Dr. P. Velon, Dr. J. Artigas and E. Thomssen. Dr. R. Marriott, immediate past president, is also a member of the Comité.

In London we saw Beauty Counselors' John and "Pat" Clifford, Reggie and Leslie Warner (John Gosnell), S.P.C.'s Freddy Wells; Jack and Olive Pickthall (I.F.F.).

In Copenhagen it was the Erik Thomssens, the Ole Petresches, the Connie Steffensen, the Robert Marriotts, Yardley's Sab Strainse, the I.F.S.C.C. officers, Miss L. P. Torrey, Alfred Herzka, Dr. W. Eckardt and Dr. and Mrs. N. Hjorth. Dr. Hjorth has just published a book on the sensitizing properties of balsams.

In Germany we saw Dr. Hermann Wilmsmann, Dr. H. Freytag and other Ondal coworkers; the Dr. Bruno Storps and Mother (who had us at lunch in her home), the Dr. D. Kastners all of Dr. O. Martens & Co.; the Clements Auers and Mr. Karl Reichelt of Olivin.

In Athens, we again met Miss Tassia Zamidou and Connie Zannis' brother.

In Cairo we were greatly surprised to run into Charlie Kircher (Kolmar) and his wife at Sheppard's Hotel. We had a happy reunion.

In Barcelona, the officers of the Spanish S.C.C. such as Dr. J. Artigas, the Gregory Susannas, Ramon and Papa Juan Visa (Floid) and the A. Contijochs were among the people we saw again.

The general feeling of the people to whom I talked was "why aren't we more careful—we may precipitate another war". Some of the people we saw were in the last one. After Mr. K. started blasting atoms again, we found people a bit bewildered and disappointed—somewhat like a boy who said his father always told the truth, then found out he didn't.

Business seemed good everywhere including the peddlers in Cairo. My hair cut, shampoo, scalp massage and hair dressing ran \$1.15 at the barber shop in the Semiramis Hotel in Cairo, one of the top spots in town.

We heard two operas, one at the Royal opera house in Stockholm and again at the Statopera in Vienna. The belly dancers at the Istanbul Hilton were listed as "Oriental Ballerinas". At a place called the Sheharazade in Cairo, we saw a show more in the native style. Our protector and guide was Sheppard's dragoman #5, a fellow named Mohamed Mahmoud. We

recommend him. Make your cash deal in advance—all costs included; but don't visit his relative's shop across the street. Mohamed knows his ancient history of the area.

But Mr. Nasser could do a lot in the interest of efficiency and tourism by getting a little more work out of the immigration and customs boys. The coins could be marked in both languages as are the bills. You never know what you have in coins because of the markings.

Beirut is a very pleasant place to visit. We stayed at the St. George hotel on the sea. Everything here is excellent but the beef. The Kirchers, mentioned earlier, were going there on their way home.

Wherever you go, you see U. S. cosmetics, imported as is or made in the particular country. If anything, they are more vigorously promoted than domestic brands. One man told me that only U. S. cosmetics can be sold in his country. Domestic brands are considered inferior. Taxes plague the broader sale of cosmetics in many countries.

My reading material consisted mainly of galleys of the *Chemistry and Manufacture of Cosmetics*, Vol. I, and *S.C.C. Journal* material. I finished off five back issues of the *Listener* and the paperback, *Early Christianity*, by Baintor. Now I'm back at the desk and grinding again.

Check List of Best Selling Technical Books

COSMETICS, SCIENCE AND TECHNOLOGY. The editorial board of this encyclopedia cosmetic work is made up of H. D. Goulden, E. G. Klarmann, and Edward Sagarin, executive editor. It is in five parts: I, Scope of Cosmetics (80 pages); II, Toilet Preparations (812 pages containing 800 formulas); III, Manufacture and Technology (214 pages); IV, Physiological Considerations (92 pages); plus preface and complete index. The sixty-five experts who contributed, are a "who's who" of cosmetic chemists in the United States and Canada. 1433 pages. Illustrated. Price \$27.50.

HENLEY'S 20TH CENTURY BOOK OF FORMULAS, PROCESSES, TRADE SECRETS—REVISED, ENLARGED EDITION. Manufacturers, chemists and others call HENLEY'S the most valuable book of its kind. Nearly 10,000 formulas, processes, trade secrets. It contains formulas for nearly everything imaginable; new ways of doing things; technical process; so-called trade secrets. It has helped thousands make more from their present business and professions. A single formula may be worth more than 100 times the price of the book. Over 900 pages, completely indexed, cloth binding, \$5.25 postpaid.

PRESSURIZED PACKAGING (AEROSOLS). By Alfred Herzka, Jack Pickthall. Although technical problems occur with all types of packages, those which arise with pressurized packages are many and complex. This reference book, by two recognized authorities deals with propellants, containers, valves, filling methods, laboratory procedures, emulsified systems, and perfumes. There is a complete section containing more than 200 formulations, including foods, insecticides, cosmetics, paints, and numerous other products. 400 pages. Illustrated. Price \$15.00.

PERFUMERY SYNTHETICS AND ISOLATES. By Paul A. Bedoukian. This carefully compiled volume meets the genuine need for authoritative data on perfumery synthetics. It embraces the history, chemistry, physical and chemical properties, manufacture, uses, and other pertinent data of the principal perfumery compounds; and covers the important perfume synthetics. A complete index adds to the value of this important work. 488 pages. Price \$10.25.

THE HANDBOOK OF SOLVENTS. By Leopold Scheffan and Morris Jacobs. The most useful work of its kind today. Part I covers theoretical aspects and practical attributes such as solvent action, solvent power, evaporation and evaporation rates. In Part II the physical constants of over 2700 liquid compounds are tabulated for easy comparison. 728 pages. Illustrated. Price \$12.00.

COSMETICS—THEIR PRINCIPLES AND PRACTICES. By Ralph G. Harry. discussed the skin, its nutrition and scientific care; the hair, its proper grooming, the physio-chemical problems involved in its washing; the teeth and their care, covering the present status of different dentrifices, and the luster-producing properties of ingredients. Much of the information has its source in the research activities of its author, embracing chemistry, dermatology, and microbiology. 786 pages. Illustrated. Price \$17.25.

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- INTERNATIONAL ENCYCLOPEDIA OF COSMETIC MATERIAL TRADE NAMES.—\$7.50
- HANDBOOK OF COSMETIC MATERIALS.—\$14.50
- THE ESSENTIAL OILS. (Specify Volume)
- MANUAL FOR THE ESSENCE INDUSTRY.—\$8.25
- AMERICAN PERFUMER DOCUMENTARY.—\$5.00

INTERNATIONAL ENCYCLOPEDIA OF COSMETIC MATERIAL TRADE NAMES. By Maison G. deNavarre, brings you reference data you will turn to constantly . . . the most complete listing of all the materials of the world used in cosmetic manufacture . . . including quick concise descriptions of approximately 4,000 materials . . . the names and addresses of the suppliers . . . and a very useful cross-index of the materials and their uses. You will use it when seeking new materials, or substitutes for those you may now be using. 400 pages. Price \$7.50.

HANDBOOK OF COSMETIC MATERIALS. (Their Properties, Uses, and Toxic and Dermatologic Actions). By Leon Greenburg and David Lester. Contains alphabetical listing, with frequent cross references, of information on approximately 1,000 substances. For each compound gives: formula (including collateral names), properties, toxic action, dermatological action. Exhaustive bibliography. Essential for manufacturing chemists, cosmetic industry, dermatologists, allergists. 467 pages. Price \$14.50.

THE ESSENTIAL OILS. By Ernest Guenther, with the collaboration of leading experts, this monumental six-volume work includes: Vol. I, Origin and Development of Essential Oils. 427 pages. Price \$9.50. Vol. II, detailed data on several hundred constituents of essential oils. 852 pages. Price \$13.50. Vol. III, discusses the oils of the plant families Rutaceae and Labiate. 777 pages. Price \$13.50. Vol. IV, covers the widely used oils: citronella, lemongrass, bois de rose, cassia, and others. 752 pages. Price \$13.50. Vol. V, takes up other oils of special interest to flavor, perfume and soap manufacturers: rose, ginger, cardamom, anise. 507 pages. Price \$13.50. Vol. VI, completes the monographs on individual oils: wintergreen, sweet birch juniper berries, and the numerous pine oils. 552 pages. Price \$13.50.

MANUAL FOR THE ESSENCE INDUSTRY. By Erich Walter. Comprises methods, with formulas for making all kinds of essences for liquors and alcoholic drinks, fruit juices and jams, mineral waters, essences for fruits and other vegetables, essences for confectionery and pastry. Describes raw materials and laboratory practice. Discusses taste and the transfer to foods and beverages. 427 pages. Illustrated. Price \$8.25. Published 1916.

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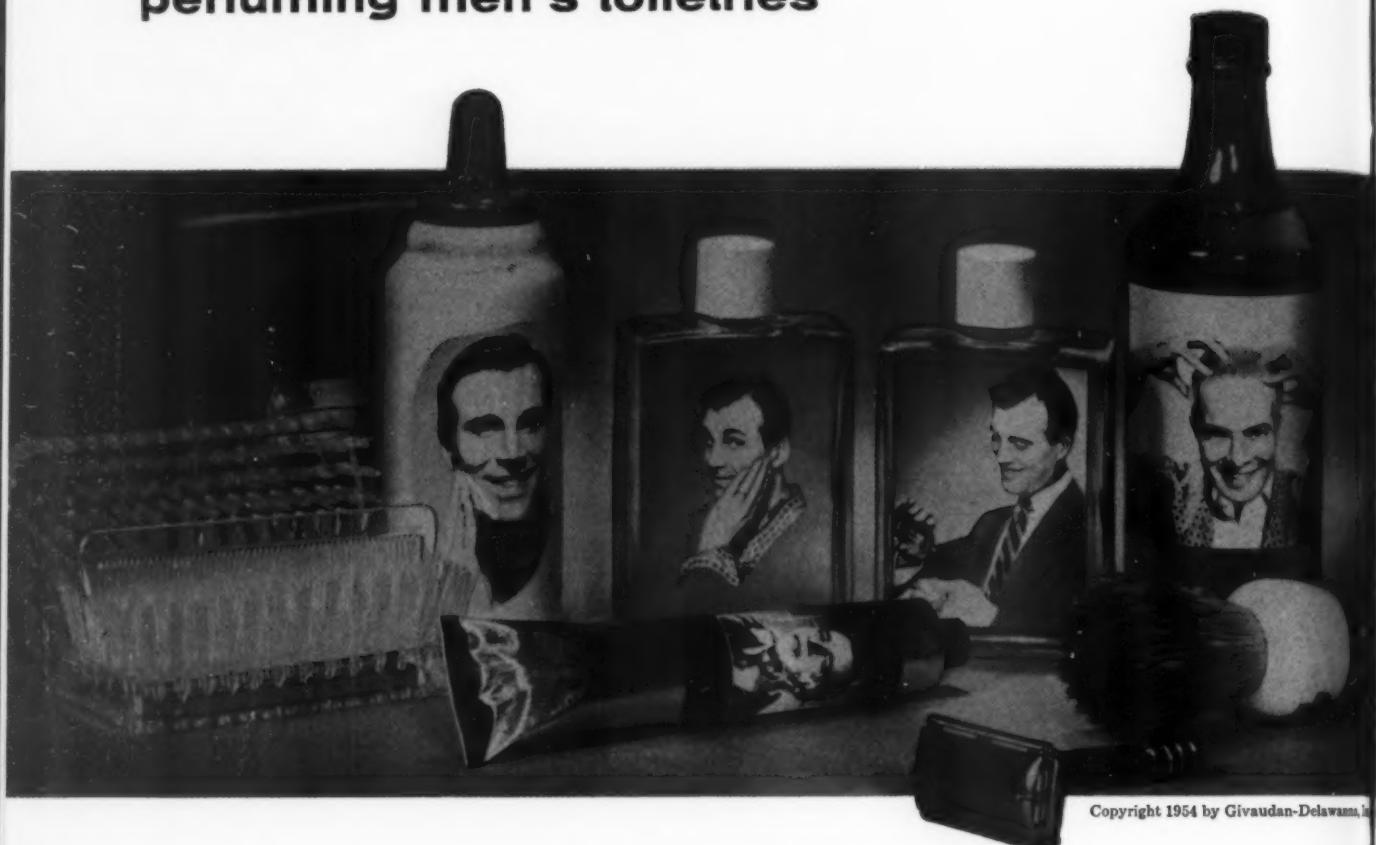
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Key Properties of Starches

BY OTTO WURZBURG, Associate Director, Alexander Laboratories and WILLIAM HERBST, Supervisor, Starch Applications Research, Alexander Laboratories National Starch and Chemical Corporation

ORDINARY AND MODIFIED STARCHES have a large endowment of useful properties. Different industrial processes utilize separate groups of these properties, so that articles on the technology of starches frequently do not seem to be based on the same or even related products. The articles, of course, reflect the interests of a specific industry. Cosmetic and pharmaceutical firms, paper and textile mills, laundries, bakeries and other starch consumers quite naturally view starches against a background of their own requirements.

The authors feel that there is value in this restrictive approach, for today starch and its modifications are specialty products. In this article they therefore examine the properties of starches that are of particular benefit to pharmaceutical and cosmetic manufacturers. The properties are based on the behavior of starch as an intact granule; a swollen granule; a dispersed granule; a film former; and a nutrient and chemical raw material.

Starch as an intact granule: Starch is produced in the seeds, tubers and roots of plants, where it is stored as reserve carbohydrate. Each plant creates starch granules, or cells, that differ from those of other plants. Depending on the plant source, the granules vary greatly in shape and size. Rice starch, the smallest of the granules, is polygonal and has a diameter of 3 to 8 microns (25,400 microns = 1 inch). Corn starch is either polygonal or round and has a diameter of 5 to 25 microns. And potato starch, which is oyster shaped and the largest of the granules has a diameter of 15 to 100 microns.

The average surface area of a pound of corn starch is roughly 4000 sq. ft. and that of 1 pound of potato starch approximately 550 sq. ft.

These data reveal that the starch granule is tiny and has a large surface area—a combination that gives starch excellent sorption properties. As a sorption agent, starch is further enhanced by such properties as edibility, white color, purity, low cost and availability, which also make it valuable as a diluent.

The granules are moderately porous and are easily penetrated by moisture. In addition starch is a polyhydroxy compound; the hydroxyl groups have an affinity for the water molecule. Starch, therefore, is a particularly good sorption agent for moisture.

The granules, which may be regarded as microscopic packages of starch, are also insoluble in cold water. They are extracted from their plant sources by a simple cold water process, which is reflected in the high purity and low cost of starch. The amount of moisture that starch absorbs varies with the humidity and temperature. For example, at 20% relative humidity and 72°F., corn starch will absorb 9% of its own weight; at 66% relative humidity and 72°F., 16% of its own weight; and at 90% relative humidity and 72°F., 21% of its own weight.

Although the granules are insoluble in cold water, they absorb hot water or steam and swell. On swelling, the granules lose their intact nature and with it many desirable properties. For this reason, ordinary starch granules are not used in applications requiring steam sterilization or hot water.

Several modified starches have been developed in

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which the granules are toughened to resist the swelling action of hot water and steam. Such modified starches, for example, the highly crosslinked^[1], are used for dusting powders, foot powders and rubber dusting. Crosslinked starches have also successfully been used in aerosol products. The propellant causes ordinary starches to swell. Because of their inertness, crosslinked starches resist swelling.

A unique modified starch is produced through the introduction of hydrophobic (water hating) groups in the starch molecule. Starches containing hydrophobic groups are water repellent, that is, they resist wetting. They are used as a pre-shave powder with electric razors and as dusting powders in humid climates.

One of the more interesting properties of hydrophobic starches is that they absorb moisture even though they repel water. The moisture absorption, however, does not cause the clumping that occurs with ordinary starches. Hydrophobic starches^[2] have proven valuable as processing aids for removing moisture during the manufacture of pharmaceuticals.

Starch as a swollen granule: During cooking, the granules absorb many times their weight of water. The amount of water that is absorbed depends on the nature of the ordinary or modified starch. After the granules have absorbed the maximum quantity of water, they form a paste. This paste is used for thickening pharmaceutical jellies and salves and as a suspending agent in cosmetics.

What happens to the starch granules on prolonged cooking? We can follow their progress by heating a starch slurry to 200°F. At about 160°F. the bonds holding the granules together are weakened. The granules start to swell. They imbibe water and blow up to as much as 50 or 60 times their original volume.

As the swelling continues, the clarity of the mix increases. Its viscosity rises until the granules have reached maximum hydration. Further heating and agitation causes the granules to rupture and collapse. They lose their hydrating ability, and the viscosity of the paste starts to decrease.

Cause of molecular dispersion

The collapse of the granules causes the starch molecules to form a molecular dispersion. On standing, the dispersions of some starches become increasingly opaque, and their viscosities increase. The clarity and viscosity of other starch dispersions remain relatively unchanged.

The polymeric architecture of the starch molecule governs the behavior of the dispersion. Structurally, starch is a carbohydrate made up of anhydro glucose units. It is chemically identical to glucose but differs in the way that the anhydro glucose units are linked together.

Starch contains two polymers. One is *amylose*, in which the anhydro glucose units are linked end-to-end in a relatively linear structure. The other is *amylopectin*, which also contains anhydro glucose units linked end-to-end, but in addition has branches.

The amylose molecules generally contain between 200 and 1000 anhydro glucose units. The amylopectin molecules are considerably larger. Their exact size

is not known, but estimates range as high as 200,000 anhydro glucose units.

Amylose molecules frequently line up in parallel bundles. This association (coming together of similar molecules) is intensified by the linear structure and the attractive force exerted between the hydroxyl groups of adjacent molecules.

Conventional starches, such as corn, wheat, rice, etc., contain 18% to 28% amylose. This highly associative polymer is responsible for the tendency of such starches to thicken, or gel, on cooling. Conversely, amylopectin does not readily gel. The large size and branched structure of these molecules prevent them from closely associating.

Waxy corn and waxy sorghum yield starches that are essentially pure amylopectin. Dispersions made from these starches show very little tendency to gel on cooling.

A dispersion of highly swollen granules which contains the normal mixture of both polymers possesses a short, salve-like consistency—a highly desirable property that is utilized for thickening pharmaceuticals and cosmetics.

Unfortunately because of the sensitivity of the granule to rupture and the variations in the rate of swelling of different granules, the highly swollen state is transient in most ordinary starches. This deficiency has been overcome, however, by crosslinking starch through the introduction of glycerol, phosphate, citrate or similar groups.

Crosslinking greatly increases the strength of the bonds that hold the granule together. Even mild crosslinking produces a starch whose granules are significantly resistant to rupture. They lose their critical vulnerability to the normally harmful action of high mixing shear, hot water and many chemicals. Severe crosslinking intensifies this effect. In the extreme, crosslinking produces a starch with the strength to resist the swelling action of hot water. Some starches are crosslinked and then further modified to improve such properties as stability at low temperatures, viscosity, or hydrating capacity, and clarity.

Although crosslinking in most modified starches is small, the toughening is indeed profound. The toughened, swollen granule is transformed into an ideal thickening agent for salves, ointments, jellies and lotions.

Starch as a dispersed (ruptured) granule: Fully dispersed starches are excellent suspending agents for such products as calamine lotion, barium carbonate suspensions (for gastrointestinal fluoroscopy) and medicated gum candies. In order for starch to be used in these applications, which utilize the properties of the ruptured granule, it must be extensively modified.

Ordinary starch is a weak emulsifier. However, through the addition of hydrophobic groupings, the emulsifying ability of ordinary starch is greatly improved, and excellent oil and water emulsions are obtained. Some of the oils that are emulsified by modified starches are mineral oil, castor oil, vitamin oils and flavor oils. Even such hydrocarbons as benzene, toluene, hexane and kerosene are readily emulsified by these starches. Starch-based emulsions

have excellent shelf stability and good consistency and lubricity for skin applications.

Starch as a film former: When a starch dispersion dries, the molecules are deposited as a film. The strength of the film and its binding capacity are functions of the size and shape of the starch molecules and the nature of the chemical groupings.

High molecular weights and linearity favor strong, tough films. However, high molecular weights require the use of the starch at low concentration, which makes it necessary to evaporate large amounts of water prior to film formation. The presence of excess water also slows down the rate at which the binding strength is developed. Further, as discussed in the section *Starch as a swollen granule*, linear molecules tend to associate producing gels, which give their dispersions poor handling characteristics.

A tug of war is created: those properties of starch that are needed to produce a tough, strong film—high molecular weight and linearity—also contribute undesirable characteristics to the film.

To overcome this chemical conflict, it is common practice to reduce the size of the starch molecule by acid hydrolysis, oxidation or pyroconversion. Many hydrolyzed starches are used in the manufacture of pills and medicated gums and in pan coating and enrobing medicated candies. A good range of such starches is available, enabling manufacturers to vary the rate of solubility of the coatings.

The film forming properties of starch are also used to bind components of tablet formulations. An important example of the binding ability of starch is the preparation of encapsulated water insoluble oils. In these products, the starch film forms a protective coating that contains the oil.

Starch as a nutrient and chemical raw material: Starch is readily digested by body enzymes. It can be safely assimilated in those applications where it is deliberately or accidentally taken into the body. In addition, because starch is a carbohydrate, it is a controlled source of glucose for use as a nutrient in some fermentations.

The hydrolysis of starch into glucose is a reaction in which the starch has the unusual role of a chemical raw material. Glucose is prescribed nutritionally and medicinally for both humans and animals. It is also used in the manufacture of sorbitol, an alcohol that is widely employed in the pharmaceutical and cosmetic industries.

Starch as a specialty product: A large number of ordinary and modified starches are available to cosmetic and pharmaceutical formulators. Such properties as viscosity, color, emulsifying capacity and taste are today controlled by the starch manufacturer. Some of these properties are relatively independent. Others are interrelated, so that an improvement in one property may produce changes in one or more companion properties. The choice among desired properties is expanding under the impetus of product research. As indicated by the increasing use of starches in the cosmetic and pharmaceutical industries, formulators are more than ever exploiting unique starch properties for specialized applications.

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An Emulsion Study with Sweet Almond Oil

THE PROBLEMS ASSOCIATED with emulsion technology are numerous and complex. In addition, the factors affecting emulsion formation are greatly interrelated, so that very often it is not correct to say that one factor alone produces a definite effect, but rather that a composite of several renders an emulsion "good" or "bad."

Even a limited survey of the literature reveals a tremendous quantity and diversity of work done on emulsions in the cosmetic field. These works fall in four basic areas: emulsion types, particle size, viscosity, and stability.

With the development of the HLB system, a new tool was given the emulsion technologist. Even with its limitations, the HLB system of classifying emulsifiers provided a method by which emulsifier selection could be raised from the level of a "hit-and-miss" situation to at least a semi-scientific one. The work of Griffin has provided a method of establishing HLB values for emulsifiers and required HLB values for various oils.^[1]

With this system, emulsifying agents are considered to contain both hydrophilic and lipophilic portions. The degree to which an agent contains more of one than the other of these groups dictates its effect when introduced into an oil and water system. Those acting basically as hydrophilic entities are assigned high HLB values and tend to produce O/W emulsions, while the lipophilic ones have low HLB values and encourage formation of W/O emulsions. The range extends from one to forty and any two emulsifiers added to a system are additive in action.^[1]

The required HLB values for various oils, once established, provide a guide for selection of a suitable emulsifying agent or agents whose HLB or additive HLB is proper for that of the oil phase.

Classed as a non-volatile oil, for many years sweet almond oil has been used in a variety of cosmetic products. The closeness of its chemistry to that of human sebum and the fact that it is absorbed to some extent^[2] makes almond oil particularly useful in lubricating creams and oils. Neither a primary irritant nor a sensitizer, it is not only innocuous, but a valuable emollient^[3] and the presence of 52.92% unsaturated acids facilitates emulsion formation.

Unlike many other natural oils, sweet almond oil has excellent keeping properties and its relatively low Iodine Number (93-103.4) makes it useful in the formulation of hair preparations for which Iodine values below 105 are recommended.^[4]

This work was designed to determine the HLB of

Study made at the research laboratories, Purdue University School of Pharmacy.

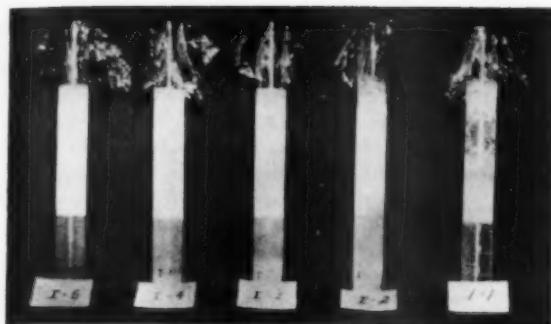


Fig. 1. Formula preparations.

sweet almond oil and to develop an improved cosmetic emulsion on the basis of the information obtained.

Following the method outlined by Griffin, six grams of emulsifying agent, fifty grams of sweet almond oil and fifty grams of distilled water were used to prepare a series of emulsions. The emulsifiers, Span 60 and Tween 60, were weighed, placed in an eight oz. wide mouth jar and the oil added. All the water was added, and the bottle was capped and shaken twenty-five times through a vertical shake of approximately 20". The emulsions produced were then placed in 100 milliliter graduated cylinders. After 24 hours, evaluations were made on the basis of creaming and/or separation.

Emulsion type determinations were made by placing several drops of the emulsion on a glass surface and adding minute quantities of F. D. & C. Red No. 2. If the dye spread over the surface of the emulsion within three minutes, the emulsion was considered to be O/W. If no spreading occurred within the allotted time, the product was considered W/O.

The various combinations of Tween 60 and Span 60 used are shown in Table 1 and the preparations can be seen in Figure 1. The combination of 4.5 grams of Span 60 (75% of the total emulsifier used) and 1.5 grams of Tween 60 (25% of the total emulsifier used)

TABLE 1

Determination of required HLB for sweet almond oil using various ratios of Tween 60 and Span 60 (Formulas I-1 through I-5) and determination of the best blend of emulgents for the determined HLB of sweet almond oil (Formulas II-1 through II-3)*

Formula No.	Emulsifying Agent	HLB of E.A.	Wt. E. A. (Em.)	Evaluation (After 24 hrs.)
I-1	Span 60 Tween 60	4.7 14.9	6.0 0.0	No Emulsion Formed
I-2	Span 60 Tween 60	4.7 14.9	4.5 1.5	No Creaming
I-3	Span 60 Tween 60	4.7 14.9	3.0	Slight Creaming
I-4	Span 60 Tween 60	4.7 14.9	1.5 4.5	Moderate Creaming
I-5	Span 60 Tween 60	4.7 14.9	0.0 6.0	Incomplete Emulsification
II-1	Span 40 Tween 40	6.7 15.6	5.6 0.4	No Creaming Not Pourable
II-2	Span 60 Tween 60	4.7 14.9	4.6 1.4	Excessive Creaming
II-3	Span 85 Tween 85	1.8 11.0	2.5 3.5	No Creaming Pourable

*The oil-in-water emulsions indicated in this table all contained 50 grams of sweet almond oil and 50 grams of water.

for 50 grams of oil produced the most stable emulsion.

In a second series, consideration was given to quantities within the range of 4.5 grams of Span 60 and 1.5 grams of Tween 60 which would result in an even more stable product than that produced with a total of six grams of the emulsifiers in the proportions indicated above. Accordingly, ratios of Span 60 to Tween 60, including 4.2/1.8, 3.9/2.1, 4.8/1.2, 5.1/0.9 and 5.4/0.6 were used to prepare five additional emulsions. None of these emulsions was considered superior to that produced with the ratio of 4.5/1.5 of Span 60 and Tween 60. Thus, this latter combination (4.5/1.5) was used to calculate the required HLB of sweet almond oil, using the formula:

$$\text{HLB Almond Oil} = \frac{W_A \text{ HLB}_A + W_B \text{ HLB}_B}{W_A + W_B} \quad (1)$$

Where HLB_A is the assigned HLB of the first emulsifying agent, HLB_B is that of the second, W_A is the weight used of the first emulsifying agent and W_B the weight used of the second.

The HLB of sweet almond oil for O/W emulsions, as determined by the formula above, is 7.25.

Determination of the most effective surface active agent blend for the determined HLB of sweet almond oil

Having established the required HLB for sweet almond oil, the emulgents which would produce the most stable emulsion of this oil were sought. Using the method described by the Atlas Powder Company^[5] and using the value of 7.25 for the required HLB of sweet almond oil, appropriate quantities of three groups of emulsifiers were used and additional emulsions were prepared and evaluated.

The formulations are shown in Table No. 1 (II-1, II-3).

As can be seen from the Table the combination of 2.5 grams of Span 85 and 3.5 grams of Tween 85 for

TABLE 2

Emulsions prepared by selected emulsifier addition methods and by variation of the oil and water phases

No.	Emulsifiers Span 85/Tween 85 (Gms.)	Wt. Oil (Gms.)	Wt. Water (Gms.)	Emulsion Type	Formula Evaluation*	Emulsifier Addition Method	Particle Size (Micron)
II-1	2.5/3.5	90	10	W/O	G	O**	8.76
II-2	2.5/3.5	75	25	O/W	G	O	6.68
II-3	2.5/3.5	50	50	O/W	G	O	5.67
II-4	2.5/3.5	25	75	O/W	S	O	5.61
II-5	2.5/3.5	10	90	O/W	S	O	
II-6	2.5/3.5	90	10	W/O	L	PMS***	
II-7	2.5/3.5	75	25	O/W	L	PMS	7.47
II-8	2.5/3.5	50	50	O/W	L	PMS	5.81
II-9	2.5/3.5	25	75	O/W	S	PMS	4.92
II-10	2.5/3.5	10	90	O/W	S	PMS	4.41

*The emulsions, prepared by two different methods of incorporating the emulsifying agents, were evaluated on the basis of how each compared to its formulation counterpart, e.g. II-1 compared to II-6, II-2 compared to II-7, etc. G = greater creaming, S = same, L = less.

**O = Both emulsifiers were added to the oil phase.

***PMS = the two emulsifiers were added to the phase in which they were most soluble or dispersible.

50 grams of oil produced the most stable emulsion.

Next, the effect on the final product of two different methods of adding the emulsifying agents was considered. The emulsifiers, Span 85 and Tween 85, were combined with 50 grams of sweet almond oil and 50 grams of distilled water by two methods.

In the first emulsions, the Span 85 and Tween 85 were both added to the sweet almond oil and the distilled water then added to this combination. In the second group, the same amounts of emulsifiers were used, but the Span 85 was added to the oil phase and the Tween 85 added to the water. The water-Tween mixture was then added to the oil-Span phase and emulsification was effected.

In addition to variation of emulsifier addition, the ratio of oil to water was also varied according to the schedule seen in Table No. 2.

Emulsion type and degree of creaming were determined as previously described.

Particle size determination was carried out microscopically using the following procedure:

1. Twenty-four hours after preparation, each emulsion was shaken vertically through 20 strokes.
2. One drop was removed, 20 drops of 50% aqueous propylene glycol added, and the combination gently mixed.
3. One drop of the resulting mixture was placed on a microscope slide and a slide cover placed on top.
4. A 15 minute waiting period followed.
5. Three complete fields were counted in three different areas of the slide and no less than 400 counts made per slide. Particle size was determined by the use of a calibrated micrometer inserted in the eye piece.
6. The arithmetic mean was calculated by the standard method.

As can be seen from Table No. 2, all emulsions were of the O/W type except those containing 90% oil and 10% water which were W/O. As the amount of water was increased, the amount of creaming in-

creased and the particle size of the oil decreased in all the emulsions. At concentrations of approximately 50% water and below, the emulsions produced were more stable when prepared by incorporating each of the emulsifiers in a different phase. Above 50%, no significant difference in creaming between the emulsions prepared by the two methods was noted.

Effect of mixing order on emulsion type

A series of five emulsions containing respectively, 90, 75, 50, 25, and 10 grams of sweet almond oil, 10, 25, 50, 75, and 90 grams of water and 2.5 grams of Span 85 and 3.5 grams of Tween 85 was prepared by adding each emulsifier to a different phase and the water to the oil phase in divided portions. A second series of five was prepared, differing only in the fact that the oil phase was added in divided portions to the water.

As can be seen from Table No. 3, no difference in emulsion type resulted from the two orders of mixing, nor did the mixing order greatly affect the stability of the O/W emulsions. The only stability difference noted in the O/W emulsions was at a concentration of 75 grams of oil and 25 grams of water in which case the emulsion produced by the addition of the oil phase to the water exhibited markedly less creaming.

Preparation of an emollient cream

Using the information obtained in this work, a cream intended to be used primarily as an emollient was developed.

The following formula is presented as an improved emollient cream:

Beeswax	16.3%
Light Mineral Oil	11.0%
Sweet Almond Oil	27.0%
Lantrol	1.0%
Propyl Paraben	0.1%
Span 60	5.8%
Tween 60	1.8%
Water	37.0%

Conclusions

1. The required HLB for Sweet Almond Oil is 7.25 for an O/W emulsion.
2. An O/W emulsion containing less than 50% sweet almond oil produced less creaming when the Span 85 and Tween 85 were added to the sweet almond oil and distilled water, respectively, prior to the combination of the two phases.
3. Method of addition (water to oil phase or oil to water phase) in the formula used did not affect either rate of creaming or emulsion type.
4. Using the required HLB of sweet almond oil for O/W emulsions, a combination of Span 85 and Tween 85 produced the most stable emulsion of the materials tested.

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TABLE 3						
Emulsions prepared by the use of two orders of mixing and with various ratios of oil and water.						
Formula No.	Emulsifiers Span 85/Tween 85 (Gm.)	Sweet Almond Oil (Gm.)	Water (Gm.)	Emulsion Type	Order of Mixing*	Evaluation**
III-1	2.5/3.5	90	10	W/O	W-O	L
III-2	2.5/3.5	75	25	O/W	W-O	M
III-3	2.5/3.5	50	50	O/W	W-O	S
III-4	2.5/3.5	25	75	O/W	W-O	M
III-5	2.5/3.5	10	90	O/W	W-O	S
III-6	2.5/3.5	90	10	W/O	O-W	M
III-7	2.5/3.5	75	25	O/W	O-W	L
III-8	2.5/3.5	50	50	O/W	O-W	S
III-9	2.5/3.5	25	75	O/W	O-W	S
III-10	2.5/3.5	10	90	O/W	O-W	S

*W-O = water phase added to the oil; O-W = oil phase added to the water phase

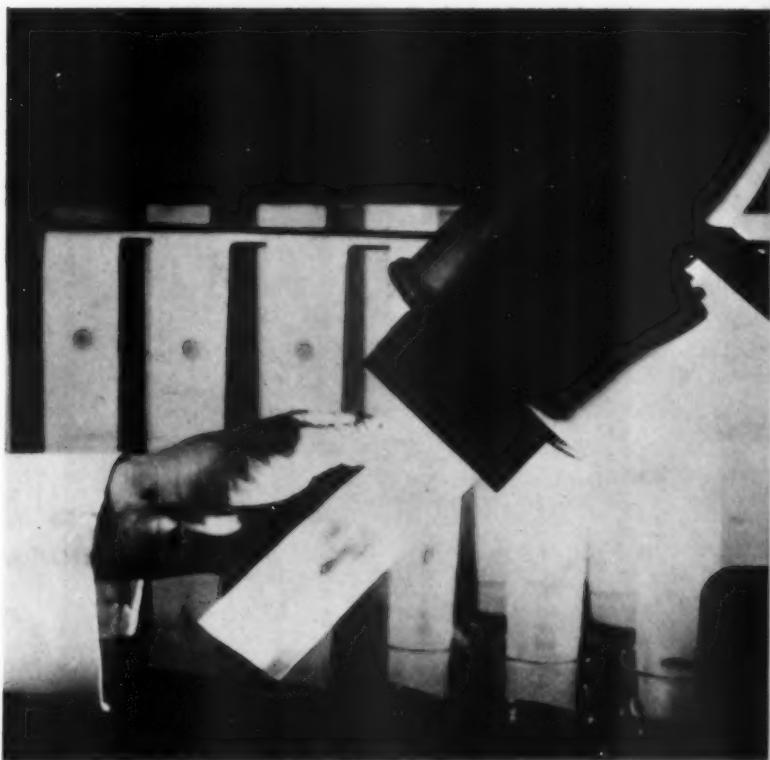
**Evaluation procedure was the same as that described in the footnote under Table No. 2.

COVER STORY

Cover Picture: Microscopic examination and identification of Botanicals by a Pharmacognosist.

Panax Ginseng

Botanicals are identified in quality control department by Paper Chromatograph and viewed under Ultra Violet light.



BY WILLIAM A. MEER, PH.D AND GEORGE MEER, JR.
Meer Corporation, New York City

IN RECENT YEARS a considerable number of preparations containing Ginseng have appeared on the European and American market, and since much publicity has been given to this "Wonder Root of Eternal Youth", it has apparently been used in Royal Jelly cosmetics, combined with lecithin and vitamins as well as similarly active materials.^[1]

Ginseng is the root of *Panax ginseng* C. A. Meyer, which is native to Eastern Asia. It grows wild or is cultivated in North Korea, China, Japan, and the Pacific coastal regions of the Soviet Union. The genus received its name from PANACEA, the Greek all-healing or cure-all. The Chinese word "GINSENG" means "human root". Roots having a human-like form are particularly valued in that area of the world.

Related to *Panax ginseng* is *Panax quinquefolius* L., found in shady mountain forests of the United States. Ginseng is adapted best to the Northeastern, North Central, and North Pacific Coast States and can also be grown successfully in the Appalachian Mountain region.

Indications are, however, that the East Asian Ginseng Root is superior to the American in its healing power.^[1]

Prior to the First World War, this country exported

approximately 1,000,000 pounds of these roots to China.^[2] Today production of cultivated Ginseng by the Soviet Union has completely supplanted the American product.^[1]

Ginseng is widely used in China as a tonic, aphrodisiac, and rejuvenative. It is apparently particularly of value in diseases which originate in disturbances of the nervous system.

An interesting review of the history of Ginseng root can be found in an article by Schliebs.^[3] The properties of "Gin-Tzaen" were recorded in the Chinese book of herbs "Schen-Nun" as early as the 3rd century A.D.

Panax Ginseng is a perennial plant, ranging in height from 30 to 70 cm. The stem is simple and straight. The flowering parts are small and dusty white in color whereas the leaves are grayish-green. The fruits are bright red berries. The root is spindle shaped, light yellow brown and may be up to 20 cm. long and up to 2.5 cm. thick. Its fracture is short, white and mealy. The bark of root contains numerous reddish resinous groups. The root has a weak odor and a sweetish and somewhat aromatic taste.^[1,4]

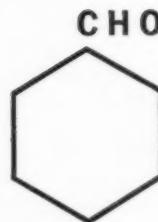
The wild root has always been more highly valued than its cultivated variety; however, Schulz^[1] reports that young cultivated roots are only 1½ to 2 times less



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active than those growing wild. Originally roots weighing between 300 to 400 gms. were available. These were over 100 years old. Roots collected more recently are much younger ranging from 10 to 40 years in age and weighing from 50 to 150 gms. The Far East is now the principle source of Panax cultivation.^[3] In 1957 more than 60,000 Ginseng plants were set out in plantations in the environs of Moscow.^[1]

This drug has been studied to a greater extent by the Soviet Academy of Science. Tests have shown that water and dilute alcohol are best suited for the extraction of the active principles of Ginseng. These types of preparations have been the most active.^[1]

The ground root has been prescribed from 0.25 to 0.50 gm. daily whereas 15 to 20 drops, 2 to 3 times daily of a 1:10 tincture are also employed. Still higher dosages have been given depending on the activity of the root.^[1]

Russian report

Russian pharmacologists report that *Panax Ginseng* stimulates the central nervous system and respiration while also regulating the activity of the heart and vascular arterial systems.^[1]

Esdorn,^[5] on the basis of Russian work done in 1953 concluded that Ginseng is most applicable in conditions of exhaustion, dyspepsia, functional disturbances of the heart and arterial system and in hypertension.

Interestingly enough Dorsch^[6] states that in World War II, the Japanese Army sought to improve the physical performance of its troops by dispensing Ginseng preparations. They apparently reported favorable results.

Earlier reports indicate that the drug contains the saponin-like glycosides, Panakilon and Kolonin. The latter was at one time thought to be closely related in composition to male semen. Investigators have isolated Panaxin, Panax Acid, a phytosterin, a phosphate, sebacic acid as well as a volatile oil (Panacen).

More recently Japanese and Chinese chemists isolated an alkaloid, B-complex vitamins, niacin, pantothenic acid, as well as steroid hormones with pronounced estrogenic activity. Russian investigators have isolated two new glycosides, Panaxosid A and Panaxosid B which they claim are responsible for Ginseng activity.^[7] These may be the substances previously mentioned as Panaxin and Panax Acid.

Unfortunately, *Panax Ginseng* has not been investigated to any great extent for its potential use in cosmetic formulations. The great deal of interest aroused recently in its physiological activity and constituents, however, promises to correct that condition. There would certainly seem to be a place for a drug which has a reputation for being a tonic, stimulant, rejuvenative, euphoric and aphrodisiac.

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Is Bergamot a Sensitizer?

BY ROBERT E. HORSEY, President
Essential Oil Association of U. S. A.
and Vice President Givaudan-Delawanna, Inc.

I WELCOME THE OPPORTUNITY of discussing on behalf of the Essential Oil Association, the serious subject of listing oil of bergamot as a strong sensitizer under the regulations of the Federal Hazardous Substances Labeling Act.

This is a serious subject because it is the first time that a specific perfume material has been singled out by a government agency as an offending substance in consumer products.

The Essential Oil Association's concern about this listing goes further than just oil of bergamot as it may be used as a precedent to black-list or place restrictions on other perfume materials.

I will separate my remarks into two parts: (1) One dealing with the activity of the Essential Oil Association; and (2) My personal opinion of how we may be abetting further restrictions on the use of perfumes and perfume materials under present or new legislation.

To give you the proper perspective on the Essential Oil Association's activity, it is necessary to repeat the background of the Federal Hazardous Substances

Labeling Act. Some of us had followed the drafting of this law through trade associations such as the Chemical Specialties Manufacturers Association and the Manufacturing Chemists Association. It is important to understand that industry supported this legislation and over the years has voluntarily placed cautionary labeling on consumer products which presented a hazard.

No industry complaint was made on the term or definition of strong sensitizer in the law because it specifically states "before designating any substance as a strong sensitizer, the secretary upon consideration of the frequency of occurrence and severity of reaction, shall find that substance has a significant potential for causing hypersensitivity."

The Act was passed on July 12, 1960 and proposed regulations were issued on April 29, 1961. From the uproar which the industry made, you can understand the dissatisfaction with these regulations. Perhaps the bitterest pill was the fact that in spite of industry's cooperation in drafting the Act, they were not consulted on formulating any of the regulations. As you know, oil of bergamot was listed as a strong sensitizer without limitation, if one molecule was present in a product it would require cautionary labeling. This

Address before American Society of Perfumers, Sept. 20, 1961

was a shock to all of us and though we were aware that photo-sensitivity reactions were reported due to bergamot, none of us believe this occurs frequently.

The Essential Oil Association's first action was to have the chairman of its Scientific Committee meet with FDA's Pharmacology and Dermatology Group. This discussion brought out two facts.

1. Oil of bergamot was so listed on the recommendations of an advisory panel of six dermatologists.

2. Neither the FDA and evidently neither did the advisory panel have any statistical data indicating the frequency of occurrence.

The Essential Oil Association then surveyed its membership about its use and experience with oil of bergamot. With a usage of 75,000 lbs. annually, no adverse experience was reported in handling bergamot over many years. Only one company reported a customer being involved in a consumer complaint on oil of bergamot dermatitis.

The Essential Oil Association filed formal protest to this listing and also prompted the consorcio in Italy to protest which they did through the Italian Commercial Attache.

We feel these protests resulted in the revision of this particular regulation. It now reads that oil of bergamot and products containing 2% or more of oil of bergamot are strong sensitizers. This is a ridiculous situation since oil of bergamot is rarely if ever sold as a household item and it is inconceivable that any household product might contain 2% or more of bergamot. Frankly, there is no sensible basis for this listing since there are no consumer products involved. But there is one important fact which must not be overlooked. Another section of the regulations points out that cosmetics are exempt under this act but they may be regarded as mis-branded under the Food, Drug & Cosmetic Act, if they offer a substantial risk of injury from any handling or use that is customary or usual.

Precedent for further restrictions?

The listing of bergamot as a strong sensitizer in the Hazardous Substances Labeling Act may give FDA the precedent to apply the same standard to cosmetics. This is our primary concern especially when you consider the statements appearing in the August 7, 1961 issue of *Food Chemical News*. It stated the dermatology panel endorsed FDA's definition of strong sensitizer and commented that a "strong sensitizer" causes sensitization in one or more persons in 10,000 population, or less if the sensitization is severe. How anyone could determine whether a product is a strong sensitizer under this definition is beyond comprehension. Certainly no one could afford a clinical study of this magnitude. But even if you did run a test on 10,000 individuals, it would give you a result which would preclude oil of bergamot. Spoor and Traub in their article "Skin Reaction to Cosmetics" published in the *New York State Medical Journal* show statistical data indicating that if one were to pretest 30,000 individuals and find no adverse reactions, still one in every 10,000 of the general population would be likely to show sensitization.

What further action the Essential Oil Association will take, I cannot advise you since we have not had

time to reach a decision. Personally, I feel that all of us should do everything we can to prevent arbitrary listing of any ingredient under any law. I urge those of you working for companies making consumer products, to get your trade associations and companies to protest any unreasonable legislation.

Certainly we are all anxious to have safe products, but if we are going to try to make products which will not cause reactions to those few highly susceptible individuals, then we had better throw in the sponge right now.

Now as to my personal opinions and again may I emphasize they do not reflect any discussions or opinions of the Essential Oil Association membership. Further, I assure you there are no personal or commercial motives involved.

Unsupported statements in literature

It is my sincere opinion that members of our industry, be they suppliers or buyers, too frequently take the printed word as gospel and consequently follow a course of action which in the long run is not to their best interests, and I'm certain some of them are sure to haunt us in the future. Let me give you some examples of what I'm referring to.

1. An advertisement appeared on a new perfume material some few years ago which stated this product did not have the irritating properties of hydroxy-citronellal. As far as could be determined no factual clinical study was made to substantiate that hydroxy was irritating or that the new product was less so. The basis for the statement was references in the literature stating hydroxy was irritating.

2. In the British Pharmaceutical Journal an article appeared on Essential Oils and Aromatic Chemicals. In one part of the article the author listed the oils and chemicals as known to cause irritation. Once again through inquiry, it was learned neither the author or company had any data to support this listing, but were quoting various statements appearing in the literature over the years.

3. Referring to this so-called literature, many cosmetic chemists and others use Greenfields & Lesters *Handbook of Cosmetical Materials* as a source of information on dermatologic action. A great deal of time was spent tracing the references given by these authors. Perhaps there were as many as a dozen references given on a single perfume material, but as so often occurs one reference quoted another reference and it was impossible to find a basic clinical study substantiating the irritation or sensitization. Certainly there were isolated cases reported by dermatologists, but in so many instances it was questionable if the alleged offending material was determined as the cause of the patients' dermatitis. Some other statements appearing in the literature are, "most cosmetic preparations producing dermatitis do so because of their perfume content". Another states, "a rule of thumb recommendation to follow in any perfume material is to say that the more susceptible the aromatic to oxidation, the greater the tendency to smart the skin".

I am not taking the position that perfume materials cannot cause a hypersensitivity, but you cannot gen-

eralize from a few cases that they should be eliminated from all cosmetics.

Fortunately there are some good articles published such as the one by Dr. Ed. Masters in the *New York State Medical Journal*. This paper showed a summary of a major cosmetic company's experience on complaints. It represented 113 plus million units sold in 18 different cosmetic categories. The average number of reactions were 0.4 per 100,000 units. In the case of colognes and perfumes which would be expected to have the highest percentage of perfume oil, the reactions were .02 per 100,000 units. Certainly this would seem to be far less than one reaction in 10,000 individuals, since this represented sales over a number of years.

4. Manufacturers and promoters of non-allergic or hypo-allergic cosmetics give the impression in their promotional material that perfumes are a major cause of dermatitis from cosmetics.

5. Compounds are offered for sale which are claimed to least likely cause sensitization and to not contain primary irritants. It is difficult to assess these claims since no statistical data is available on the incidence of dermatitis reactions from cosmetics perfumed with the commonly used perfume oils. But this is not the important point. Here again, implications are made that perfume materials are prime offenders in causing allergic reactions from cosmetics. Promotional material on these compounds state, "there is, in fact, really only a very limited number of naturals as well as synthetic substances that never cause any allergies at all". This type of statement could also be made about almost every ingredient used in cosmetics. What we need are facts and not statements which are meaningless and I quote again, "this research work did not yield exact results".

All of these examples have been given to emphasize one point—if we within the industry continue to indict perfume materials as bad actors, being harmful, irritants and sensitizers, we most likely will convince the jury of consumers and regulatory agencies to condemn them and place restrictions on their use. I am not pleading for use of materials indiscriminately but before we condemn one, let's have evidence which is substantial and conclusive. Let's avoid the habit of giving equal value to one dermatologist's report on a few patients versus the millions of cosmetic units sold each year. Let's stop quoting references unsupported by well designed scientific tests.

Greatest service from joint survey

In the not too distant future it is my opinion we can expect revision of the present Cosmetic Act which will include more rigid standards for safety of use. Some of our utterances may backfire to cause us needless labeling, additional investigative expenditures and revision of products.

Probably the greatest service which could be rendered to our industry would be a survey made jointly by the cosmetic manufacturers reporting by category the number of packages of cosmetic preparations sold and the number of complaints of irritation received and identifying, if possible, the cause of irritation. Though this might appear to be an onerous task, it would be of immeasurable value to prevent unwarranted attacks on the products of our companies.

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A Practical Course for Training Creative Perfumers

BY WILLIAM LAMBERT

AS THE PERFUME, toilet goods and cosmetic industry continues to grow—both in sales and in product variety—there is developing an urgent need for an increased number of expert creative perfumers.

The task of increasing the ranks has been an industry problem in recent years. A skilled perfumer must have a sound working knowledge of: the numerous raw materials (both natural and synthetic); of their physical and chemical properties; and also of the many chemicals essential to the creation of intriguing fragrances. This is a big order, but is only the beginning for to this knowledge the skilled perfumer must contribute an inborn, creative talent to blend the ingredients into appealing and well-rounded compositions.

That this industry need is being met is evidenced in the success of the course on Perfumery and Essential Oils given at Rutgers, the State University's Extension Division in Newark, N. J. The course, which was started four years ago, is in direct contrast to U. S. industry practice "inherited" from the European industry.

In Europe, a novice learns the art and science of perfumery by serving a long apprenticeship under a skilled perfumer for whom he acts as assistant, just as an aspiring artist does under the tutelage of a master painter. In this atmosphere, genius and creative talent of a novice is most likely to be discovered and then developed. In somewhat the same way creative perfumers have been developed in the United States.

But such methods leave much to be desired. Knowledge of the many raw materials needed in the creation of fragrances is usually acquired by the novice in a tedious and often incomplete way. Moreover, new techniques are developed and new materials are found from time to time, and a watchful eye must be kept on the unpredictable and frequently changing public tastes. Such information is more accurately and more promptly supplied by a well informed, experienced expert who has made it his business to keep abreast of such matters than by the master-apprentice method. Consequently, he is able to guide novices and help them develop any natural creative ability they may have.

New views and ideas

The courses at Rutgers provide new viewpoints and ideas for the creative perfumer and the closely allied, creative flavor chemist.

The courses are under the direction of Steffen Arctander, scientist and author, whose experience covers 18 years of practical perfume and flavor work in Europe and the United States, coupled with information acquired during seven trips to Africa for new material.

The course in perfumery extends for two years. It is made up of two semesters of 16 weeks each, consisting of two hours of lectures and two hours of laboratory work once a week, for a total of 256 hours. The class meets Monday evening from 6:15

to 10:15. The third semester in the perfumery course started October 2. It covers descriptions of raw materials, identification and other techniques. It is a practical course, for the students determine the effect of individual materials by actual trial. In this way the student learns what is right and what is wrong, and which of several materials in a given case produces the best affect. Thus, the novice learns how to avoid errors. In a single semester each student examines between 200 and 300 raw materials. Each material is first shown and then a perfume with and without that material is presented for comparison so that a choice may be made. This method is used for raw materials generally, including both familiar and new synthetics.

Industry sponsors the course

The course on Perfumery is sponsored by about a dozen leading companies, making it possible to reduce the tuition for each student. All students come from companies in the industry, and each must be currently working in the field. This includes those who take only the basic course inasmuch as they are engaged in buying and selling raw materials.

The new course on Flavor Materials which began October 4 will continue for ten weeks. All major techniques will be demonstrated along with new experimental flavors hitherto unexploited. This makes up a large part of the course.

The major textbook in the perfume and flavor courses is "Perfume and Flavor Materials of Natural Origin," by Arctander, published in 1961. The 736 pages contain information gathered by the author from research stations, universities, distilleries, growers and exporters in many parts of the world. Also in-

cluded is the author's almost complete collection of perfume and flavor materials of natural origin. The data is presented in dictionary form and relevant information about each material is given in clearly understood terms. The book is illustrated with color photographs taken by the author. Sections include definitions and methods of processing, monographs on raw materials, tables on tonnages and value of world production of the more important natural perfume and flavor materials, and a French-German-Spanish condensed index plus a complete index in English.

Instructor Arctander's colorful career

Steffen Arctander, who conducts the courses, has had a colorful career. He was born in Denmark in 1919 and was graduated from the University of Copenhagen as a pharmacist. In later post graduate study he earned the degree of Diploma Pharmacist (equivalent to a Ph.D. degree) in 1943.

During World War II he instructed sabotage groups in high explosives at night for the British Intelligence Service. In 1944 he was arrested by the Gestapo, but with characteristic ingenuity and courage managed to escape. For the next 13 months he lived and worked in the underground. He joined a pharmaceutical firm that had an essential oil department. Here he developed a department for making synthetic aromatic chemicals. He continued in that work for five years and then joined Co-Ro Mfg. Co., where for six years he served as perfumer and flavor chemist. In 1957 Arctander came to the United States as a perfumer for the Colgate-Palmolive Company, and in 1959 joined International Flavors and Fragrances, Inc., New York City, as head of the odor quality control department.

Lever Brothers gives \$1500 to equip first university perfume laboratory



When the new science building on the Newark campus of Rutgers University is completed it will house a perfume laboratory, the first university project of its kind in the United States. Lever Brothers has donated \$1500 to the Rutgers Newark Extension Center for equipment in the perfume laboratory. Dr. Willard M. Bright, (left) research and development vice president of Lever Brothers, presents the check to Dr. Mason W. Gross, president of Rutgers (right). Watching is Dr. Ernest E. McMahon, dean of Rutgers University Extension division.

Abstracts of Papers Presented at Symposium on Cosmetic Problems in General Practice, Committee on Cosmetics, American Medical Association Dallas, Texas, November 8, 1961

Cutaneous Cleansing in Health and Disease

Raymond R. Suskind, M.D.

*Dermatologist of the Kettering Laboratory;
Associate Professor, Department of Preventive
Medicine and Dermatology, University of
Cincinnati, Cincinnati, Ohio*

Medical and cosmetic problems about which the general practitioner or dermatologist is consulted, frequently involve the choice and proper use of skin cleansing methods. It is appropriate therefore, that this thesis concern itself with such matters as:

1. the usefulness of cleansing techniques in maintaining normal structure and function of the skin.
2. types of cleansing agents and their indications.
3. modes of action.
4. soaps and synthetic detergents as preventive and therapeutic agents.
5. the adverse effects of skin cleansing.
6. what to do about the skin which appears to be intolerant to soaps.

It would also be appropriate to discuss some of the common superstitions and misconceptions which doctors, as well as their patients, have regarding the uses of soaps and other cleansing measures.

Facts and Fancies on the Care of the Hair and Nails

Albert Kligman, M.D., Ph.D.

*Professor of Dermatology,
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania*

Facts and fancies about the care of the hair and nails will be discussed. The anatomy and normal functions of these structures will be briefly outlined. Special consideration will be given to the degree to which the health and vitality of these structures can be preserved and manipulated by modern science.

Dermatitis Due to Cosmetics

James W. Burks, M.D.

*Professor of Clinical Dermatology, Tulane
University, New Orleans, Louisiana*

Dermatitis from cosmetics can be expected to continue as long as there is an allergic component of the population, and as long as new products appear

and old ones are altered. Diagnosis of cosmetic dermatitis is not difficult if a reasonably high index of suspicion is maintained, and if some of the classical reactive patterns are recognized.

Federal regulatory measures and voluntary controls of the cosmetic industry have made cosmetic products fairly safe for general use. Further development and expansion of these controls are necessary, however, to minimize existing hazards and prevent new ones as changes in products occur. Primary irritation, less of a problem than sensitization, can probably be further reduced by eliminating deterioration by time, reactions to containers, and from improper use.

Skin Protection in the Household and on the Job

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Skin is the dynamic interface between man and his environment. It is possessed of numerous physiologic attributes, among which is the unique action of replenishing, in part, its own protection integrity. However, many materials encountered at work, in the home, or in recreational pursuits, can alter this natural defense mechanism. Proof of this is reflected in the large number of skin diseases caused each year by occupational and nonoccupational contactants.

Environmental stimuli can injure the skin through a variety of chemical, physical, and biological forces. Similarly, the cutaneous effects may be manifested in any one of a number of ways, to include a mere discoloration, a mild or severe inflammatory lesion, or a tumorous growth.

The cause and effect relationships known to exist between the antagonists within the environment and the skin have led to the development of many protective devices to avert cutaneous injury. Efficient application of skin protectives can assist in the restoration of the altered physiologic processes which accompany contact dermatoses. Conversely, an ill-chosen device or material can perpetuate the disease. Therefore, greater emphasis must be directed toward better understanding of the limitations as well as the advantages associated with skin protectives.

Suspension

Systems

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WE MAY DEFINE A SUSPENSION as a two-phase system in which the continuous (or external) phase is a liquid and the dispersed (or internal) phase is a solid. Now the dispersed phase may be discrete individual particles or there may exist a varying degree of interaction between these particles through to a complete lattice network. Thus we can encompass the following pharmaceutical dosage types: Lotions, Magmas, Mixtures, Mucilages, Gels, Jellies, Suspensions.

First we must mention basic primary controls, applicable in varying degrees to all pharmaceutical product forms, as a reminder that these controls are equally important here.

Thus the chemical purity of the raw materials, or more strictly, the limits of the impurities present, offer no unique problems. Similarly the sterility, pyrogen content, etc. must obviously be considered where applicable.

The perfect suspension offers no problem in obtaining an analytical sample for following normal chemical stability levels. Failing perfection, the stricture "Shake Well" is as vital for obtaining an analytical sample as it is for dispensing of a uniform therapeutic dose.

We can classify suspensions by end use dosage form. We then have: Parenteral Preparations, Oral Products, Aerosol Suspension, Soft Gelatin Capsule Contents, High Solid Pastes, Cosmetic Lotions.

Using our dosage form classification of suspensions, we shall briefly consider a few of the unique problems of each.

Parenteral preparations: We have a sub-class here which should be briefly mentioned. Certain powders are supplied dry for suspending just prior to usage. For such, the important consideration is its ease of suspension without agglomeration after storage. Any floccule formation could lead to needle blockage. A visual sedimentation type examination is probably most applicable here to follow any tendency in this direction; it is extremely unlikely that powder particle size will change in the dry state.

For those normally formulated as suspensions there are other problems that arise. We are now concerned with the possibility of crystal growth by solution exchange, since some solubility always exists. For this, a direct particle size distribution analysis as a function of age is essential to determine whether growth is occurring.

Higuchi^[1] has pointed out dramatically the effect of particle size on solubility, as calculated from thermodynamic first principles. Thus, considering perfect cubes, of density 2.0 molecular weight 200, and interfacial tension 50 ergs/cm.², he has shown that

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the following increases in solubility occur over that of the gross product as a function of edge size alone.

Edge size 1.0 microns	1.01 times
0.1 microns	1.08 times
0.01 microns	2.2 times

Another factor of importance in leading to crystal growth is the use of amorphous, glassy, or even metastable crystalline forms of the solid phase. The metastability may have been introduced just by the particle size reduction procedure used. Any metastable form has greater solubility than its stable form.

Growth will be impeded by use of only stable forms, with the crystals presenting the minimum total edge length, and with surface energy held at a minimum. This latter term is best controlled by influence of the other components in a solvent. Thus Swintosky^[2] has shown that he could control the solubility of procaine penicillin G in the range 0.036 through 7.06 mg./cc by suitable choice of a buffer, common ion, and a solvent moderator.

Usually sacrificial growing of particles will be of little importance. However, in a formulation which sediments, it is this solubility interchange which leads to caking aggregation by cross bridging of particles in intimate contact.

Low solid suspensions, e.g. 5% solids, generally behave as Newtonian Liquids and so are uninteresting. Higher solid contents lead to pseudo-plastic behavior. We shall discuss the rheology of depot preparations later as an example.

Oral Preparations: We are here concerned with an additional factor in suspension stability, the esthetic appearance of the product. Any physical separation, be it creaming or sediment action, is undesirable. Need for the restriction of the "Shake Well" label introduces some uncertainty as to the uniformity of the dosage. Any tendency to caking is extremely undesirable.

It is safe to say that all oral suspensions are normally poured from bottles (unless the squeeze bottle has entered here too!). In either case, the product must be mobile enough to dispense. This subject of rheology will be discussed later.

Aerosol Suspensions: The next class to be briefly mentioned represents a relatively recent newcomer to the field. Many of its problems are known to most of us by hear-say, but the literature is somewhat sparse.

Aerosol suspensions may loosely be broken in two groups. Those which are solid powders in a mixed propellant system and those which are intended to have some mist character after the flash-off of propellant.

Seldom, in this area does one achieve a stable solid in liquid suspension. Moreover, since in general use, the container is opaque, the suspension must be readily reconstituted. Such testing must be done visually in clear bottles or by direct analysis of various fractions expelled through the valve.

The real advantage of this dosage form lies in those preparations which must be maintained in a very dry condition. Such a condition may readily lead to partial agglomeration of the suspension by static charge effects. If appreciable adhesion to container walls occurs, then again the accuracy of a metered

dosage may suffer. If appreciable agglomeration to form lumps occurs, then plugging of the valve constrictions may readily result.

Since in most pharmaceuticals, the aerosol will be packaged in glass, the medium is essentially electrically insulated. This provides for the ready building of a static charge.

As in the case of parenteral products, rigid particle size control must be exercised on raw materials. With limiting the opening of a metered valve to put a maximum of about 70 microns on the smallest constriction, it is safe to say that no particle should exceed 50 microns and at least 90% should be below 25 microns.

As for the container itself, the metering devices are usually rated to $\pm 10\%$, and on demand can be $\pm 5\%$. There is very little more that can justifiably be asked.

Source of stability danger

There is one source of stability danger that must be examined. The very nature of metering valves requires gaskets of some form of rubber. Therefore a product incompatibility may exist. In extreme cases this might not show unless the bottle were stored inverted to provide liquid contact with the gasket.

In addition, for pharmaceuticals, the problem of sanitary assembly or sterilization of the valve assemblies before use must be considered. In some cases a solvent wash may be dictated.

Soft Gelatin Capsules: At first glance you might say, this certainly is not in the province of this talk. The capsules are not. However, many are filled with fluid or semi-fluid suspensions, and therefore the formulation of the suspension must assure uniformity until capsule loading.

High Solids Pastes: Again we encroach onto another speaker's domain, if only to emphasize the problem of the continuum existing in going from a low solids content suspension, to a high solids content. If the viscosity of the continuous phase is low, the suspension is obviously a fluid. If the viscosity is high, then the suspension is a paste.

A paste is then subject to the same limitations, to a lesser degree, as other suspensions. If it sediments, some of the liquid continuous phase may be visible, this is "bleeding". As with a fluid suspension, particle interaction may lead to caking.

Cosmetic Types: Most cosmetic types, even though they may contain some components which have remained solid throughout the manufacturing process, are really solidified emulsions. That is, they were suspended as emulsions at elevated temperatures, and one phase partially or completely solidified while cooling, usually with accompanying turbulent stirring.

Some of their inherent problems thus lie in the quality of their formative emulsion. The solidification process has, however, introduced the opportunity of particle interactions that were not open to the original unmelted solids. Thus a continuous semi-solid lattice may be built, which is really characteristic of a gel, but which is still very fluid.

This type is particularly susceptible to the vagaries of consumer acceptance, and hence visual stability is essential.

Being a child of an emulsion, it can at times exhibit lineage by tending to cream, particularly if appreciable air is brought in during emulsification.

General considerations

Coatings: Our first consideration is the chemical compatibility of vehicle and suspension. There are times when known incompatibilities are circumvented by coating the particles with some suitable material. The quality of the coating thus becomes critical.

The direct approach to this is the repeated leaching of such coated particles. The more elegant approach is the microscopic examination. The trained microscopist can readily evaluate the quality of the coating, as to voids, fissures, etc.

The use of normal accelerated aging techniques presents somewhat of a problem in this field. Elevated temperature implicitly brings with it increased solubility of the solid and a lower viscosity for the medium. These can be expected to contribute to greater chemical instability. *Thus the validity of Arrhenius plots for extended shelf life do have to be considered carefully.* In general, these factors will lead to a predicted shelf life for chemical stability appreciably shorter than will occur.

This can be especially true for coated suspensions. Elevated temperatures, beyond those normally anticipated for field exposure, may weaken the coating sufficiently so as to imply that it would offer no long range security, when indeed it might be very suitable.

Microscopy: In the hands of the amateur or semi-skilled operator, the microscope is an invaluable aid. In the hands of an experienced person it is an extremely powerful tool.

Although the use of the microscope for even semi-routine particle-size analysis verges on the cruel and inhuman, it is the only acceptable reference method for the calibration of other procedures more adaptable to routine usage.

Even when particle size distribution and surface area have been determined by one of the many procedures open to us, no one can deny that it only requires a cursory examination to determine the type of powder one has: -crystalline, irregular, fragmented, amorphous etc. In many cases this knowledge is essential to adequate understanding of the system.

Correlated with other bulk properties microscopy helps to give a clear insight into the changes occurring with aging in cosmetic lotions.

Sedimentation: Free settling of particles in a fluid medium is given by Stoke's Law

$$v = \frac{2r^2 (\rho - \rho_0) \delta}{9\eta_0}$$

$$= \frac{d^2 (\rho - \rho_0) \delta}{18\eta_0}$$

where v is the settling velocity of the particle under the force of gravity g in a fluid of viscosity $\eta_0 - \rho$ and ρ_0 are the densities of the particle and the fluid respectively, while r and d are the radius and diameter of the particle in question.

Now in a complicated system the value of η_0 is often replaced by η_p the viscosity of the over-all product. Since, as we shall see, for most suspension

systems of reasonable concentration the viscosity is a function of the shear rate, the appropriate value to use is very questionable. The introduction of additional proportionality constants is surely empirical.

An alternate method for considering the gravitational settlement of hindered and concentrated system has been proposed by Higuchi^[1]. This might be considered the reverse situation, the flow of the liquid medium through the suspended particles. Using the theory of fluid flow through packed beds he derived an equation for the rate of settlement,

$$v = \frac{(\rho - \rho_0) \delta r^2}{9\eta_0 K} \cdot \frac{\epsilon^3}{1-\epsilon}$$

of the liquid-powder interface where K is the Kozeny-Carman constant, and ϵ is the porosity of the bed, (the volume of liquid divided by total volume), and hence $(1-\epsilon)$ is the volume fraction of solids.

Where Stokes Law predicts uniform settling rate, this now shows us that as the suspension becomes more dense, the rate of interface settling drops rapidly.

Centrifuge: The inherent stability of a given suspension is difficult to evaluate as a physical entity. Perpetually, people seek to evaluate on a short term, the long range properties that will be encountered.

One of the frequently attempted time shorteners is the centrifuge because it seems so simple and so logical. If a certain degree of separation occurs under gravity in 30 days, then one might hope that the same level should occur in one-tenth of a day, 2½ hours, at 300 g's of centrifugal separation. Unfortunately it usually doesn't quite work, the laws of simple hydrodynamics assume unhindered free fall with no particle to particle interaction. For concentrated suspensions this is not the case. This does not rule out the centrifuge however. For a given system, it can usually be calibrated to equivalent shelf life without too much difficulty. For minor formulation changes, it may even serve as a useful guide as to direction.

Suspension stability

Certainly, if the suspension is stable to high speed centrifugation, one is quite confident that long range stability will follow—assuming the vehicle also doesn't age, deteriorate by one means or another. Thus Levy^[2] showed that gum systems may markedly lose body with aging, both for sodium alginate and sodium carboxymethyl cellulose suspensions.

Particle Sizing: The measurement of the particle size of powders has now reached such a stage that whole chapters of books, and even whole books^[3] are now available to cover the multitude of experimental methods available. Rather than single out one or two for special mention, I will just mention one recent facet of this problem, the sizing of aerosol suspensions.

Irving Porush, in the recent monograph on Aerosols^[4] states "Routine particle-size determinations are required as a control on manufacturing techniques. The stability of all suspensions should include a determination of the particle size, since a change in particle size may have a direct effect on the ther-

apeutic value of the aerosol preparation." The literature is quite clear that certain droplet sizes are most efficacious for penetration and deposition, for example 0.5 to 7 microns for pulmonary depths.^[6]

The aerosol method developed by Mintzer and Kanig^[7] is perhaps the best of the several available. This utilizes the concept of the rate of settling of particles under stirred air flow, the rate being determined photometrically.

Zeta Potential: We will now turn, for a few minutes, to a subject of possible value in the field of pharmaceutical suspension stability, electrophoretic measurements, commonly called zeta potential. For many years the colloid chemist has known that suspended particles were either positively or negatively charged, and as such behaved entirely in a manner predictable by combined electrical and hydrodynamic theories. Fine particles could either be suspended or flocculated by control of the effective particle potential, frequently by pH control alone. Intuitively, or by training, the formulator has utilized this phenomenon frequently in the developing of successful suspensions for a given suspending system^[8]. In the non-text book pharmaceutical literature utilization of zeta potential studies is infrequent. One of the best of these is that of Stanko and DeKay^[9]. Here zeta potential measurements, made by rate of particle movement under an applied electrical field, seemed to give a measure of the stability with various agents of 5% sulfamerazine suspensions. These workers found that the addition of benzalkonium chloride to a suspension reduced its zeta potential and at a critical value, here 29 mv., flocculation occurred.

An important facet of this study was the observation that in suspensions of low zeta potential, there was settling followed by caking. With sodium C.M.C., aging showed a decrease in zeta potential which was paralleled by increasing sedimentation rates. It would seem from this study that there are probably times in which valuable guidance towards successful formulation may reasonably be anticipated from zeta potential studies.

Degree of Sedimentation: Two approaches to quantitating the quality of a suspension are worthy of mention here. One is the use by DeKay^[10] of a slow but effective shaking device to permit an accurate determination of the number of shakes required to redisperse a test suspension. This is a particularly valuable measure of caking.

Another approach is to follow the rate of sedimentation. This can be done visually by measurement of sediment volume. A somewhat more sophisticated approach is the use of a sedimentation balance. Data from one such study^[11] shows that various suspending agents at the same concentration show markedly different suspending abilities. More important, different agents at the same viscosity level, show very different suspending powers, probably because of zeta potential effects.

Rheology: Several times, in discussion of specific dosage types we have mentioned rheology lightly and then passed by. In Figure 1, we see rheograms obtainable from a rotational viscosimeter. Curve A

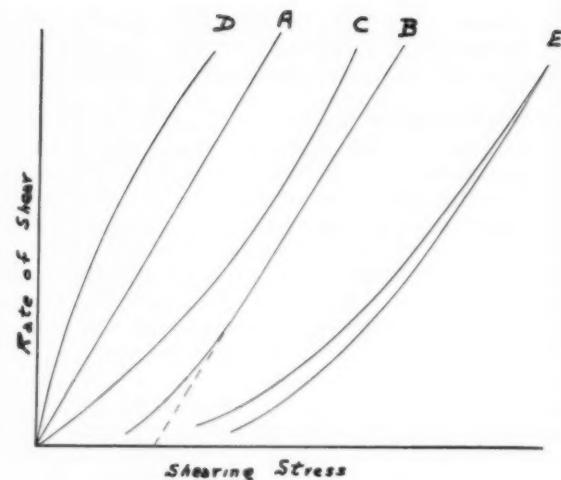


Figure 1. Typical rheological curves.

is a Newtonian. Most liquids are Newtonian through a wide shear range. The co-tangent of the line is the viscosity by fundamental definition. Alternatively the slope or tangent is defined as the fluidity. Now in B the Newtonian is considered to be displaced, we have the Bingham body system with what is defined as a yield value, the extrapolation of the linear portion to the stress axis. In curve C we see the normal pseudo-plastic curve, while in D the dilatant system. In C the viscosity steadily is dropping and in D it is increasing.

When in a pseudo-plastic system on reversing shear, a hysteresis loop is formed, we have a curve like E. It is the shape of curves that dictates the flow character of the suspension system. Thus a high yield value but low Bingham viscosity would be difficult to pour from a bottle but easy to spread. Now pourability is a combination of yield value and a fluid viscosity term. Considering classic examples, ketchup is reasonably fluid, (once it gets rolling!) but molasses is proverbial. The viscosity characteristics are potentially quite critical in certain applications. Kost-enbauder^[12] has calculated estimates for shears encountered in various operations.

Pouring 53 sec.⁻¹ (range 10-100 sec.⁻¹)

Nasal Spray Plastic Squeeze Bottle 2000 sec.⁻¹

If we consider spreading by hand, we have for a linear motion of 25 cm./sec. a shear of 250 sec.⁻¹ for a 1 mm. film and of 2500 sec.⁻¹ for a 0.1 mm. film. Similarly for needle flow, we consider the case of various gauge needles.

Table I. Shear Rates in Needles for Delivery Rates of 0.25 cc/sec. and 0.50 cc/sec. (Assuming maximum velocity at needle centre, zero at wall.)

Gauge	Wall	Internal Diameter	0.25 cc/sec. Shear Rate	0.50 cc/sec. Shear Rate
16	Regular	.047 in.	750 sec. ⁻¹	1500 sec. ⁻¹
18	Regular	.033 in.	2160 sec. ⁻¹	4300 sec. ⁻¹
18	Thin	.041 in.	1120 sec. ⁻¹	2250 sec. ⁻¹
18	Heavy	.030 in.	2860 sec. ⁻¹	5700 sec. ⁻¹
20	Regular	.0232 in.	6200 sec. ⁻¹	12500 sec. ⁻¹
22	Regular	.0158 in.	19800 sec. ⁻¹	39500 sec. ⁻¹

Empirically we^[13] have found that modern high speed production fillers may have shear rates as high as 40,000 sec.⁻¹.

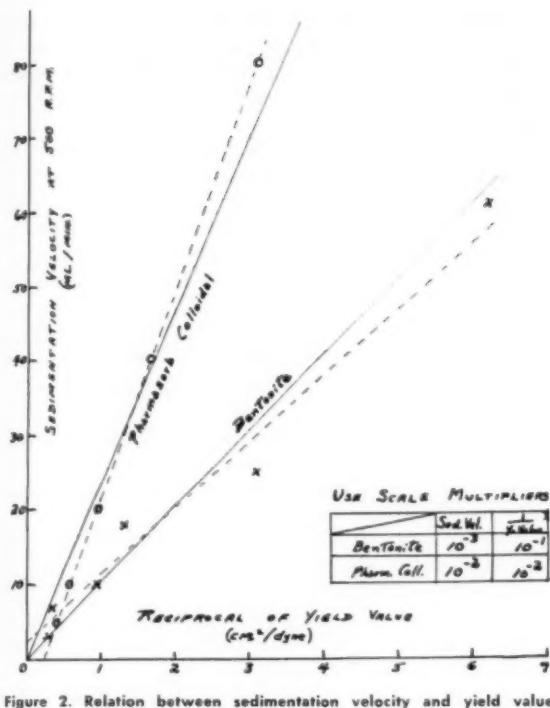


Figure 2. Relation between sedimentation velocity and yield value
 — origin line, - - - best line.

With this, let us consider the rheology of procaine penicillin G depot suspensions as reported by Ober^[14]. This report is an excellent example of the practical application of rheology to a pharmaceutical product. The rheological behavior of preparations of 55% solids with low specific surface areas showed no yield value, and on testing they were found to give flat and fanned depots, and a poor clinical rating for sustained level. Increasing surface area leads to more distinct structural break-points. In parallel, it leads to better depot shapes and to improved clinical response.

Another concept of yield value is a structural breakdown occurring after a given finite shearing. If low shear measurements are available, this breakdown is readily noted in many preparations (e.g. Heinrich and Clements^[15]).

Ober's study also included a pseudo rheological measurement, the determination of plug flow by finding the back force on a needle, in his case a 20 gauge needle, sufficient to prevent flow initiated by 200 psi gas pressure. It is very interesting to note that, regardless of yield value, narrow particle size distributions led to more readily formed plug blockage. In the broad size distributions, maximum freedom from blockage occurred for intermediate specific surface areas of the area range studied, regardless of percent solids.

Thixotropic behavior has been related to the suspending power of a medium by Martin^[16] by the relationship

$$V \cdot T = K$$

K is a system constant, T the Thixotropic area, and V the sedimentation velocity under centrifugation. The quality of this correlation is excellent for Phar-

masorb Colloidal, and reasonably good for bentonite as evidenced by straight line plots of V against $1/T$.

Meyer and Cohen^[17] vividly demonstrated the case for yield value in suspending systems by suspending golf balls, marbles and sand. Certainly the solid phase used was spectacular, and the levitation existant.

It is, then, interesting to speculate whether the Thixotropic observations of Martin *et al.* were indeed another example of the same phenomena. A similar or better correlation is seen to exist in the Figure 2 between the reciprocal of the yield value (Y.V.) and the sedimentation velocity (V), implying a relation of

$$V \cdot (Y.V.) = K$$

to be equally or even more valid. Actually, for these examples a close correlation obviously exists between yield value and thixotropy.

In a recent study^[18] of magnesia magna it was found that as shearing continued, the torque increased, a form of dilatancy. Unless violent shaking were used, the effect of this might be considered of little importance. However a control check of such a magna after high speed filling might give cause for alarm.

Viscosity and Aging: Heinrich^[15] has published some excellent examples of aging various lotions using the Ferranti-Shirley Viscometer. That lotions change notably with aging has always been the bane of a formulator.

It is therefore interesting to attempt to represent graphically the viscosity aging characteristics of a lotions type suspension.

In Figures 3 and 4 we see viscosities plotted as

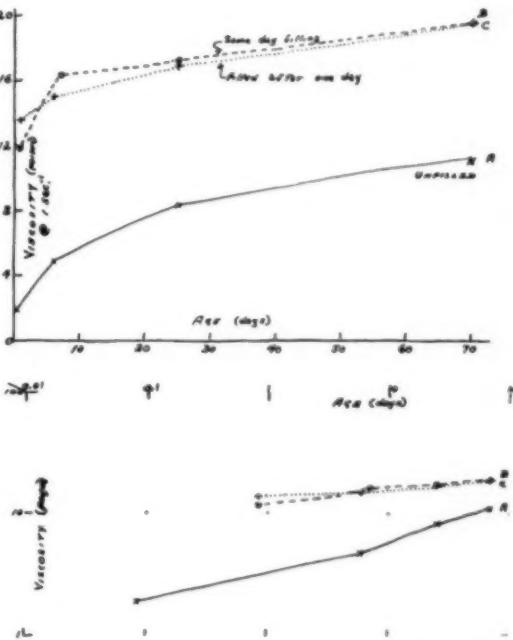


Figure 3. Effect of filling on a cosmetic lotion's rheological aging.

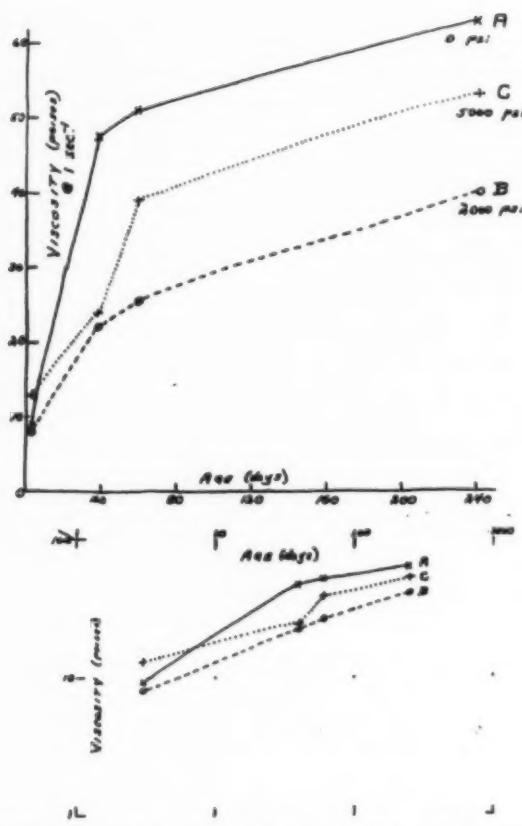


Figure 4. Effect of homogenization pressure on a cosmetic lotion's rheological aging.

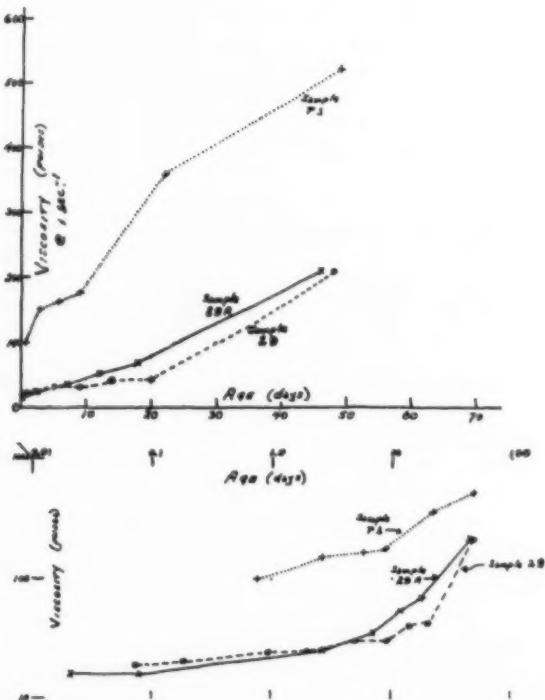


Figure 5. Rheological aging of another class of cosmetic lotions.

a function of time. In normal parlance they may be said to be levelling out in viscosity increase. In either case we would be pressed by the rectilinear plot in even estimating the viscosity at two times the last time interval seen.

However, referring to the compacting logarithmic plot the estimate seems much safer. We have come to place considerable reliance on the slopes of these lines, and in particular on breaks in them. Thus we feel that the aging characteristics of the sample A are somewhat altered by processing as evidenced by B or C.

Normally we try to follow the doubling rule for periods of observation, but this is not always practical, nor as necessary when the compacted plot is used.

The compacted plot has another virtue. It permits a review of all observations made on the sample from the initial hours to several years. Practically, the rectilinear plot cannot achieve this.

In Figure 5 for the rectilinear plot, the lines show signs of being straight with a possible tendency for some to shoot upward. The logarithmic plots more sharply show this upward tendency at an earlier time, implying that profound viscosity changes with time are to be encountered.

For those who are actively engaged in the preparation or study of suspensions, I know I have left many voids in the discussion, but I hope that I have at least reminded you of a few avenues for further thought.

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The Use of Spreading Coefficients for the Evaluation and Screening of Cosmetic Preparations

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THE SPREADING COEFFICIENT^[1] has been used as a test to determine how well one liquid will spread on another liquid in which it is insoluble. The purpose of this work was to determine whether or not this procedure could be applied in a practical way in the testing of cosmetic materials and/or finished cosmetics.

For this purpose, the work was divided into several parts. First, a number of oils of pharmaceutical and cosmetic importance were tested for their spreadability on water. Since mineral oil does not spread on water, small increments of these oils and certain surfactants were added to mineral oil to determine the effect of these substances on the spreading characteristics of mineral oil.

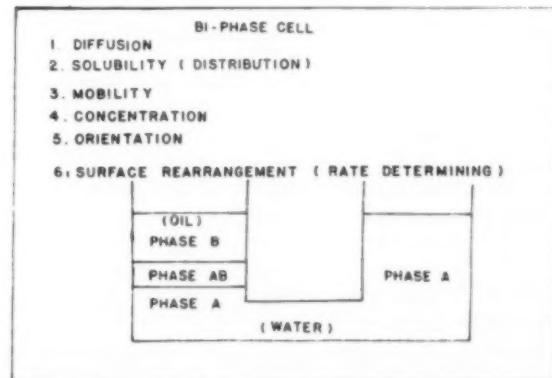
Second, a test was devised in which mineral oil was tested against a series of commercial lotions. Third, a biphasic cell was devised for purposes of studying the time relationships involved in spreading coefficient measurement.

Measurements of surface tension and interfacial tension can be related to the magnitude of spreading of one substance over another. With this in mind, the "initial" spreading coefficients^[1] for a series of oils including three surfactants were determined efficient values as a function of concentration of

the added spreader dissolved or dispersed in the oil phase were determined. Because of the poor reproducibility of these values, a biphasic cell was designed to allow for the concurrent determination of the surface tension of the oil and water phase as well as the interfacial tension between them. In this manner, the variation in spreading coefficients as a function of time could be determined by the simple and rapid ring method. (See Diagram 1.)

The relative spreadability of 18 commercial lotions utilizing a Du Nuoy tensiometer and applying the correction of Zuidema and Waters^[2]. Spreading co-

Diagram 1—Biphasic cell permits concurrent determination of the surface tension of the oil and water phase and the interfacial tension between them.



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was determined in an oil-lotion biphasic system, and an apparent constancy of spreading exists independent of time. This method is based on the inability of a solute of similar nature and similar cohesive forces to cause an appreciable change in the surface tension of the solvent.

The simplicity of the defined equations as well as the ease and rapid determination of these parameters is well suited for the evaluation and screening of lotion vehicles compatible with pharmaceutical elegance and technique.

Further work on the time relationships and applicability of the special system for lotions will be carried on in these laboratories. It would be interesting if spreading values for mixtures of added spreaders were determined, and once these values are known, it may be possible to formulate oil mixtures of definite spreading characteristics. It is possible that spreading values may be additive in nature. Further work along this line is anticipated.

Experimental

I. Spreading Coefficients

The spreading coefficients required to define these systems were calculated from the relation¹¹

Spreading coefficient = ST (Water) - ST (Oil) - IFT (Water-Oil) where ST is surface tension, and IFT is the interfacial tension. In an analogous manner the "relative spreadability" was defined as

$$\text{Relative spreadability} = \text{ST (Lotion)} - \text{ST (Oil)} - \text{IFT (Lotion-Oil)}$$

For the determination of spreading coefficients, the aqueous phase was distilled water, and the oil phase was heavy mineral oil with the added spreader. The added spreaders were common pharmaceutical oils and three surfactants which were dissolved or dispersed in the mineral oil phase.

II. Relative Spreadability

For the determination of relative spreadability of lotions, the lotion phase replaced the aqueous phase, and the oil phase was heavy mineral oil. Eighteen lotions of commercial origin were tested.

III. Normal Procedure

In the normal procedure, the surface tension of the aqueous phase is measured, the oil phase is carefully layered on the water phase and the interfacial tension is measured. The surface tension of the oil phase is then measured, and the spreading coefficient can be simply calculated with these three values after the corrections for density and ring size have been made, according to the above expression.

As an example, a 5% solution of sorbitan monooleate in mineral oil was measured against water. The surface tension of the water was 70.4 dynes/cm., the surface tension of the oil solution was 30.0 dynes/cm. and the interfacial tension was 5.0 dynes/cm. Therefore, the spreading coefficient, experimentally measured at time approximately equal to zero, or the "initial" value is

$$70.4 \text{ dynes/cm.} - 30.0 \text{ dynes/cm.} - 5.0 \text{ dynes/cm.} = +35.4$$

In both the biphasic technique and the relative spreadability technique, the spreading values were calculated as above for each system at a given time interval.

IV. Biphasic Procedure

In the biphasic technique, the normal procedure is essentially followed, except that after the interfacial tension is measured, the ring is dropped back into the aqueous phase, and the surface tensions of the oil and water phase are measured. After a given time interval, the ring is brought up to the interface and its tension is measured. Then the tensions of the other two phases are measured. The spreading coefficient as a time dependent parameter can then be evaluated. The temperature of all the above runs was 23°C. ± 2°C., all measurements being carried out in a temperature controlled room.

Table 1
Initial Spreading coefficients for a series of compounds are given at 5% W/V and zero time.

Compound	Initial Spreading Coefficient
A	40.9
B	38.4
C	36.9
D	35.6
E	33.4
F	28.6
G	24.2
H	21.3
I	19.4
J	12.6
K	11.8
L	11.7
M	10.2
N	9.8
O	2.6

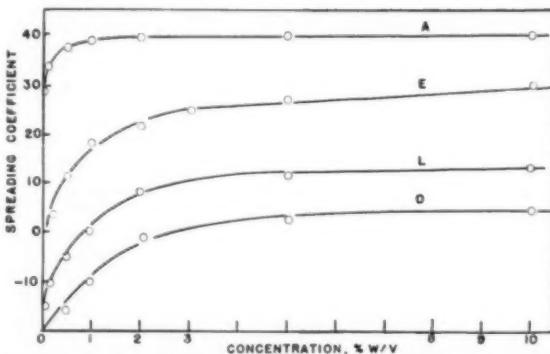


Figure 1—Initial spreading coefficients for four substances. The spreading coefficient is plotted against concentration of added spreader.

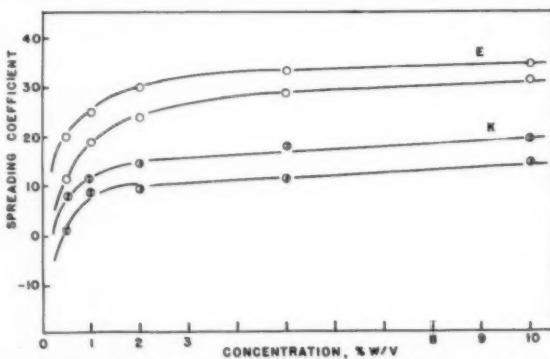


Figure 2—Reproducibility of initial spreading coefficients was fair. The variation in the two examples shown may be due to the time difference from run to run.

V. Relative Spreadability Technique

In the relative spreadability technique, both the biphasic technique and the normal technique were used, both leading to the same values, and it is felt that the normal technique can be applied more simply.

Results

The "initial" spreading coefficients for four substances are shown in Figure 1. The spreading coefficient is plotted against concentration of added spreader. The curve follows the expected isotherm^[8] and after a certain concentration, ca. 5%, an approximately constant value for spreading coefficients is obtained. The results for the eleven oils and three surfactants are tabulated in Table 1. The results are given for these spreaders at 5% W/V and at time zero.

Reproducibility of these "initial" spreading coefficients in most cases was fair, and two examples are shown in Figure 2. This variation may be due to the slight time differences from run to run.

The advantage of the biphasic cell technique is that after equilibrium is established, a constant value for the spreading coefficient should be observed. This was found to be the case experimentally, and examples are given in Figures 3 and 4. As would be expected, higher concentrations of spreaders reached this constant value in shorter periods of time.

The relative spreadability is plotted versus time in Figure 5, for a series of lotions and the results are tabulated in Table 2.

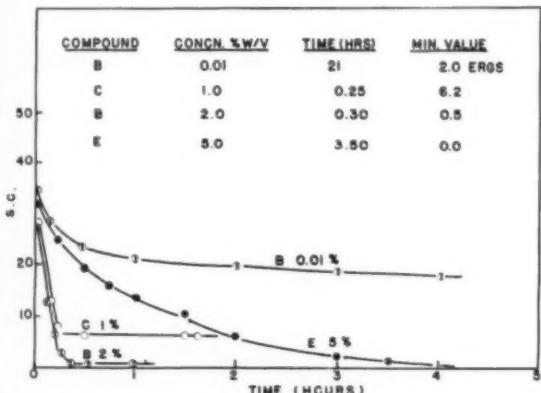


Figure 3—Variation of spreading coefficient with time, utilizing the biphasic cell.

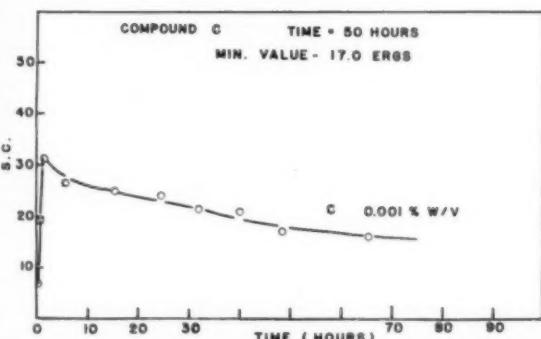


Figure 4—This plot parallels that illustrated in Figure 3.

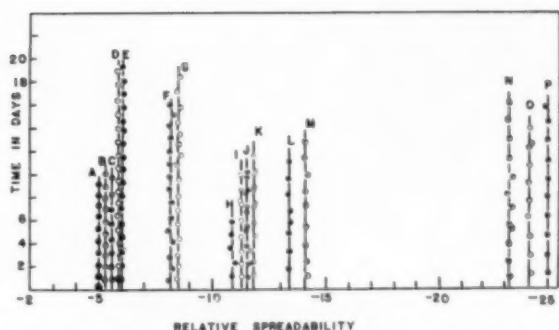


Figure 5—Relative spreadability for commercial lotions as a function of time.

Table 2
Ratios of Relative spreadability are given for a series of commercial lotions.

Lotion	Ratio	Relative Spreadability
	Relative Spreadability of Standard Lotion A ($= -5.0$)	Relative Spreadability Ratio
A		1.00
B		1.06
C		1.12
D		1.18
E		1.18
F		1.63
G		1.70
H		2.18
I		2.26
J		2.30
K		2.36
K-1		2.58
L		2.68
M		2.83
M-1		3.13
N		4.63
O		4.80
P		4.95

K-1 and M-1 are not shown in Figure 5.

Discussion

The "initial" spreading coefficients for a series of substances was determined, but the reproducibility could be considered to be, at best, fair. This variation is probably due to the time parameter, and must either be controlled or taken into account if these spreading values are to have any significance.

Many workers have investigated the time relationships of surface and interfacial tensions^{[4]-[6]} and since spreading is a parametric representation of these values, it might be expected that spreading values would be time dependent. The time variations would seem to depend on relative solubility, concentration, diffusion to the interface, surface orientation, and surface rearrangement^{[3],[4],[5],[6],[7],[8]}.

In several investigations^{[4],[7]} these authors suggest that diffusion is a rather rapid phenomenon and reorientation or rearrangement would be the rate determining step in time variability. The rearrangement of the added spreader at the interface of a biphasic system would lead to the least energetic form on the interface, that is, the most stable form.

It is felt that the biphasic technique would lend itself to time studies, since the measurement of the three parameters needed to define spreading can be obtained experimentally.

If two substances of essentially the same nature are mixed and their cohesive tendencies are similar, it might be expected that the surface tension of any mixture of these two substances would be con-



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stant and horizontally linear. There are some indications that this may be essentially correct^[10].

When a lotion of the O/W type is placed in a container, and oil is layered over it, a water-oil interface is produced. The mineral oil which is layered over the lotion is a pure phase, and although the possibility of some of the oil soluble constituents entering the oil phase exists, it would probably be minimized under these conditions. If these constituents partition themselves between the oil and the external aqueous phase of the lotion, the surface tension of the mineral oil would remain essentially constant. The surface tension of the lotion phase would also remain constant, and therefore the spreading under these conditions should be time independent, since the interfacial tension would also be constant. This was found to be the case experimentally and is shown in the noted figure.

The equation used to define this parameter is the same as the equation used for spreading coefficients, and in order to avoid confusion, the term "Relative Spreadability" has been chosen. This technique also gives relative values of spreading, for a series of lotions, as defined by the experimental conditions.

This time independent parameter would be expected to exist when the two phases are mutually insoluble in one another, diffusion from the lotion phase insignificant and the tensions of the two phases constant and independent of one another.

Accordingly, this experimental procedure has been designed so that the above restrictions are essentially correct.

Summary

1. Spreading coefficient values were determined for 14 substances as a function of concentration, restricted experimentally to time approximately equal to zero.

2. The time variation of spreading coefficients can be obtained by use of the biphasic cell technique, and an apparent constancy exists after a given point in time.

3. A system was designed which gives spreading values for lotions independent of time; the term chosen for this parameter was "relative spreadability."

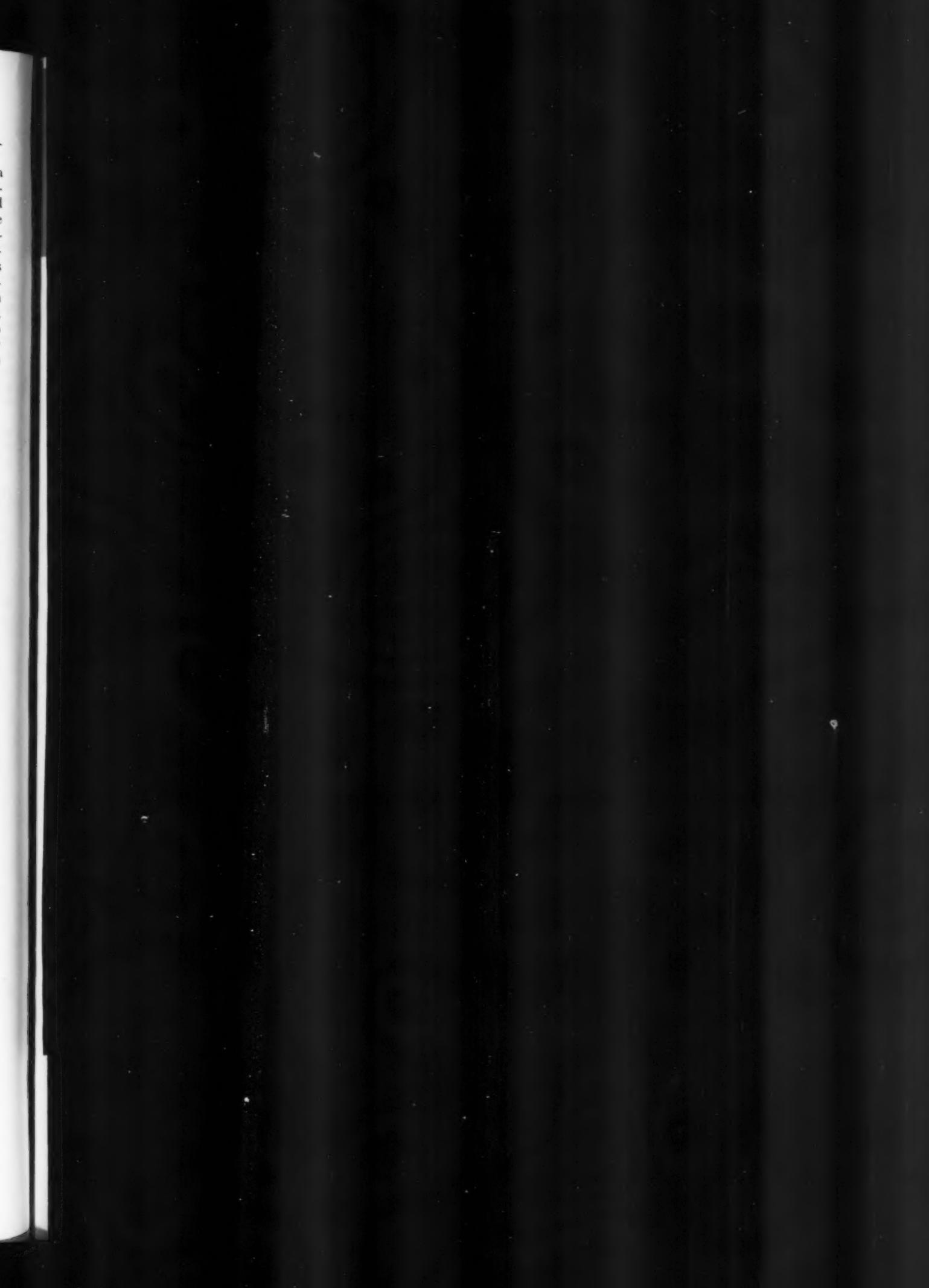
4. This system may be useful for the evaluation and screening of lotions, and may have possible kinetic usefulness.

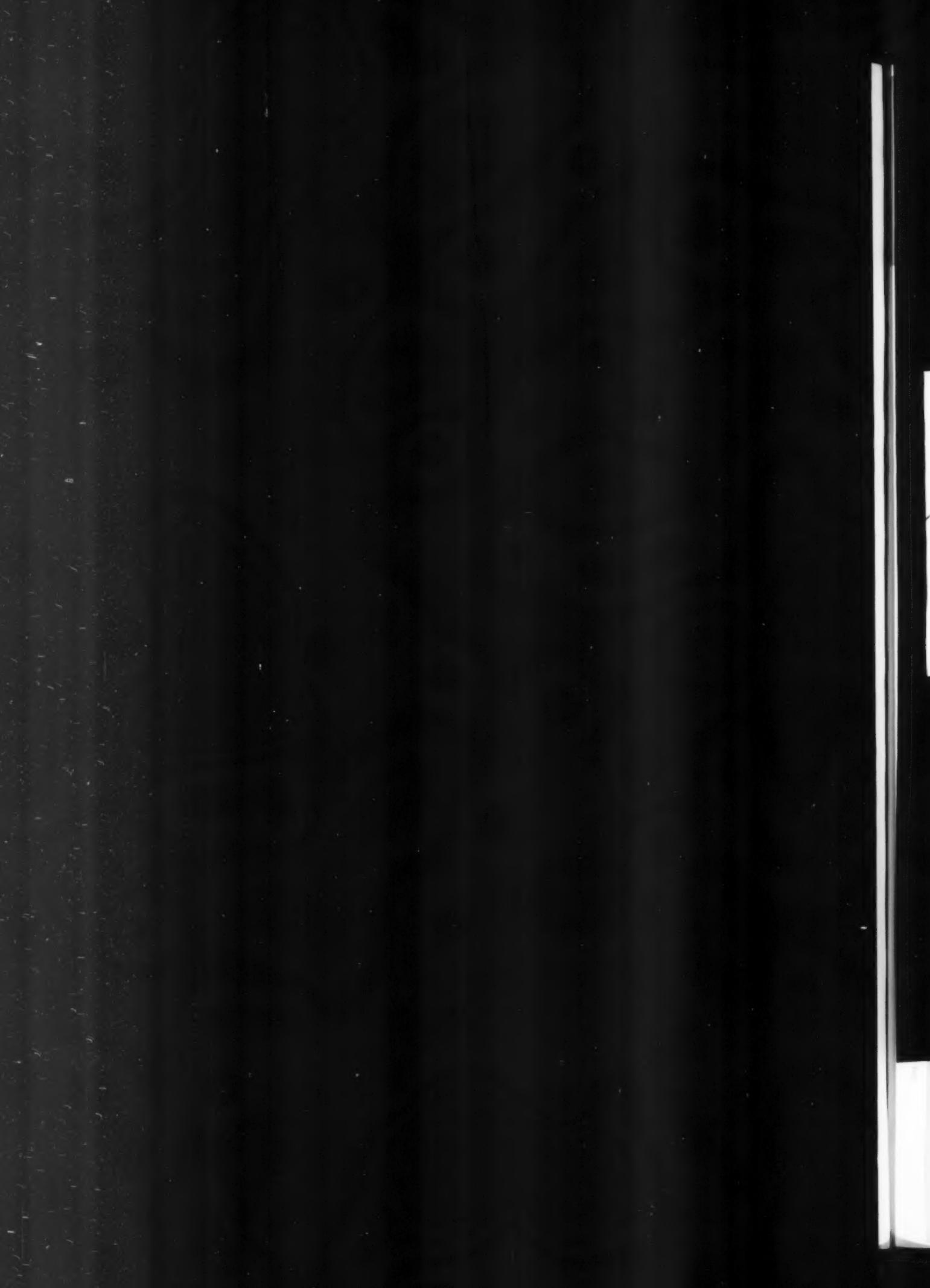
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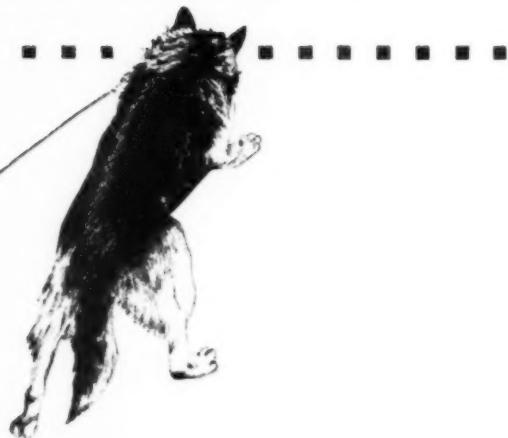
Acknowledgement

This work was supported in part by the Malmstrom Chemical Co., Newark, N.J.





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Abstracts from the 8th Annual Seminar of The Society of Cosmetic Chemists Biological Activity in Cosmetics

September 26-27, 1961

Anti-inflammatories

*Norman Orentreich, M. D.
N. Y. University School of Medicine*

The history, chemistry and methods of evaluating the efficacy of topical anti-inflammatory agents on the human skin is reviewed. The safety of such agents as well as the dissociation of topical and systemic anti-inflammatory action is discussed.

The Use of Fluorides in Anticariogenic Dentifrices

*D. S. Barrie
Procter & Gamble*

The history of fluoride dentifrices is traced, with particular emphasis on their role as a public health measure. The value and limitations of water fluoridation and topical application are discussed, and the need for an effective fluoride dentifrice is established, both as a means of extending fluoride protection to those not reached by other procedures and as a supplement to these other procedures. The early development work which indicated stannous fluoride to be the compound of choice in a fluoride dentifrice is summarized, as well as the clinical testing which confirmed its effectiveness. The manufacturer's moral responsibility to the public and responsibility under the law in the matter of safety testing of a fluoride dentifrice is treated. Finally, the implications of a recognized therapeutic product in the highly competitive dentifrice business are discussed.

All of these papers will be published in the Journal of the Society of Cosmetic Chemists. Subscription to the Journal is \$6.00 to members, and is included in the dues to the Society. The subscription price to non-members is \$18.00 per year in North America, and \$18.90 to other areas of the world.

The Journal is published nine times each year, during January, February, April, May, June, August, October, November, December. Information relative to subscriptions or memberships is available from the office of the secretary, Mr. Robert A. Kramer, 250 East 43rd St., New York 19, N. Y.

Should Sunscreens be Incorporated into Cosmetics?

*John M. Knox, M. D.
Baylor University College of Medicine*

Dermatologists have become increasingly conscious of the adverse effects of chronic exposure to sunlight. Apparently skin changes, usually interpreted as aging, are due largely—if not entirely—to sunlight. Also, fair skinned individuals who have been exposed to large amounts of sunlight have more skin cancers than any other group. The appropriate use of clothing and ultraviolet absorbers could provide protection. To date, no truly satisfactory sunscreen is commercially available to the public. Fundamental principles relating to formulating and testing sunscreens will be discussed. In our studies para-aminobenzoic acid, benzophenone derivatives, and acrylonitriles have been particularly effective absorbers.

Enzymes

*K. L. Howard, Ph. D.
Wallerstein Laboratories*

After brief considerations of the relationship of inherited characteristics to the specific activity of enzymes and of the uses of topical enzymes in medicine, cosmetic applications of enzymes are discussed. Methods for overcoming skin roughness are considered and enzymatic methods are suggested for overcoming this condition. The potential uses of keratinase are discussed in connection with various beauty preparations. Enzymes in dentifrices and the use of enzyme antagonists are also considered. The advantages of enzymes are compared with chemical agents and suggestions are given for the evaluation of enzymes in cosmetic preparations.

Effects of Estrogens on Sebaceous Glands

*John Strauss, M. D.
Boston University School of Medicine*

Various methods for measuring the sebaceous flow or output have been used in the past. In this paper, a technique which involves the direct quantitative gravimetric measurement of surface lipids trapped on ether cleaned cigarette papers is described. In the author's experience, this technique has proven to be highly reproducible for evaluating any changes in sebum production. The effect of estrogens, adminis-

tered systemically and topically to adult subjects, has been evaluated by this method as well as by biopsies. The gravimetric method has been found to be much more sensitive in respect to detecting the suppressant effect of estrogens. Sebaceous secretion is readily depressed with oral administration of doses in excess of 0.25 mg. of ethynodiol diacetate daily. Obvious undesirable systemic effects are produced by dosages of this order; therefore, systemic estrogen therapy is impractical for the inhibition of sebaceous secretion. In a further series of experiments involving the typical administration of estrogen and the combined administration of estrogens and androgens systemically, it has been proven that estrogens do not inhibit sebaceous gland activity by a direct action of the glands.

Vitamins

S. H. Rubin, Ph. D.
Hoffmann LaRoche Inc.

Evidence will be presented bearing on the utility and safety of the fat-soluble vitamins, A, D and E, which have found topical usage in medicine in the treatment of numerous skin disorders and are utilized in cosmetic formulations. Of the water soluble vitamins, panthenol is most commonly used in topical therapeutic and cosmetic products as well as in hair preparations. Evidence for effectiveness of panthenol and of its safety by oral, parenteral, percutaneous and inhalation routes will be reviewed. The conversion of panthenol to pantothenic acid and its relation to coenzyme A will be discussed. Recent data demonstrating efficacy of other vitamins by topical application will be reviewed. Of particular interest is the role of vitamin B₆ in the prevention of dental caries, which appears to be more of a local than a systemic action.



Should Bacteriostats Be Added to Toilet Soaps?

W. M. Linfield, Ph. D. and R. E. Casely
Armour & Co., Grocery Products Division

The function and significance of additives, in general, are discussed. Soap additives have to meet several requirements, namely those of usefulness, effectiveness, believability, safety and lack of adverse side effects. Bacteriostats in toilet soaps are effective as body deodorants, as degreasing agents, and lastly as an important factor in public hygiene. Effectiveness needs to be ascertained by *in vitro* as well as *in vivo* methods. The safety has to be ascertained through a series of tests carried out on various species of animals and humans. The control of anti-bacterial soaps by the FDA is discussed. There are some negative aspects to bacteriostats in soaps, particularly the possibility of resistant strains of certain organisms and the possibility of dilution of the germicidal soap concept through the use of inadequate amounts of bacteriostats. Possible future trends are discussed in terms of more active bacteriostatic agents, increased preferential adsorption on the skin, and a better understanding of the mechanism of anti-bacterial action and toxic reaction.

Skin Bacteriostat Relations

Thomas Furia
Geigy Industrial Chemicals

Concentration of various bacteriostats (hexachlorophene, trichlorocarbanilide, tetrachlorosalicylanilide and trifluoromethyl dichlorocarbanilide) on intact human skin following application from surfactant solutions has been determined. Effects of pH, bacteriostat level, surfactant type, contact time are noted. Non-uniform adsorption of bacteriostats on the skin is

Some SCC Seminar Attendees



Above: William G. Foley, Dragoco, Inc.; and Douglas Atlas, G. Barr & Company.

At Left: Edouard Hache (left) director general, Firmenich (Paris); Charles C. Bryan, president, Firmenich, Incorporated; and M. G. DeNavarre, editorial director American Perfumer.

described as well as desorption characteristics. These data are related to some inadequacies in currently used patch test techniques.

The Open Problem of Biological Activity in Cosmetics

*Emil Klarman
Lehn & Fink*

The paper proceeds from the premise that the pragmatic criterion of a "biologically active cosmetic" should be the evidence of a topical, non-traumatic, pharmacodynamic-action, either accompanied or followed by a cosmetically desirable effect, but free from any undesirable systemic involvement. Within this circumscription, the author reviews what to him appear as open problems in the areas of deodorants, vitamin cosmetics, hormone and other steroid preparations, suntan cosmetics and anti-bacterial soaps.

Anticholinergics

*J. F. Migliarese, Ph. D.
Colgate Palmolive*

One of the most promising uses for pharmacologically active agents incorporated in proprietary skin care products has been that of anticholinergics in anti-perspirant products. Unfortunately, this promise remains unrealized. Limitations such as percutaneous absorption, side effects, tolerance and marketability are presented as real obstacles in the path of successful product development. The justification for continued investigation in this area as well as the specifications for the ideal product are discussed.

Mechanisms of Bacteriostatic Action

*Eugene D. Weinberg
Indiana University*

Despite the great general similarity in both the structural components and metabolic pathways of all living cells, it is becoming increasingly apparent that sufficient specific differences occur to account for the existence of selectively toxic agents. Some of the differences consist of slight variations in the composition of permeability barriers; many of the differences are concerned with pathways of synthetic processes; only a few are associated with energy yielding reac-



Herbert Perry, Perry Brothers, Inc.; Herbert Linne and Morton Daniels, Paris Cosmetics, Inc.; and Robert Elias, Felton Chemical Co., Inc.



Pat Morone, Synfleur Scientific Laboratories, Inc.; Vincent DeFeo and Gertrude Freeze, Dodge & Olcott, Inc.; and Dr. Russell A. Cain, Pacquin, Inc.



H. Isacoff, International Flavors & Fragrances, Inc.; and Phyllis J. Carter, Atlas Chemical Industries, Inc.



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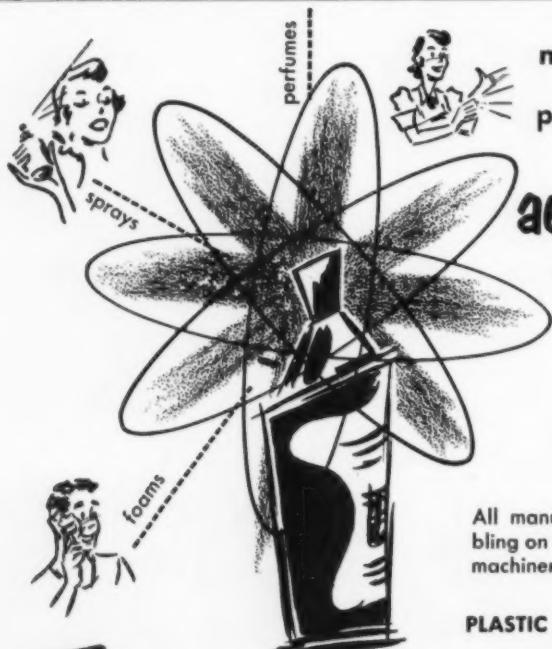


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tions. Five groups of compounds that are antibacterial in low concentration but which vary in their toxicity for man are discussed; the groups consist of compounds that (1) denature proteins, (2) disrupt lipoprotein membranes, (3) suppress protein synthesis, (4) suppress mucopeptide synthesis, and (5) compete with known essential metabolites. Topics included are: chemical mechanisms of antimicrobial action, hypotheses to explain differential antimicrobial spectra, development of and mechanisms of resistance, and side effects on the host.

Pregnenolone Acetate, a Dermatologically Active Steroid

*John Silson, M. D.
Revlon*

Pregnenolone is known to be devoid of progestational or other hormonal activity. Extensive clinical trials in arthritis and related conditions have demonstrated no systemic activity or toxicity on oral or parenteral administration. On application to the skin, however, pregnenolone has been shown to have local effects similar to the estrogenic hormones, resulting in epithelial plumping, without any of the systemic gonadal effects which limit the use of estrogens. Both effectiveness and safety have been conclusively established in repeated animal and clinical trials.

Antibiotics

*Vincent de Gennaro and R. E. Mackie
Chas. Pfizer & Co.*

With the increasing cooperation between the cosmetic and pharmaceutical industries, there is a trend towards the inclusion of biologically active ingredients in cosmetic preparations. The versatile nature of a specific group of antibiotics suggests these agents may find additional applications in this growing area of products. The properties of these essentially non-systemic antibiotics and the rationale for their possible inclusion in cosmetic preparations will be discussed. Neomycin will be singled out, to illustrate the development stages necessary in going from a pharmaceutical compound to a safe and effective deodorant product. In addition, the data collected to meet the requirements of the Food and Drug Administration will be outlined.

More SCC Seminar Attendees



**Norman W. Jones and Warren R. Godfrey,
Fritzsche Brothers, Inc.**



**S. B. Mecca, Schuylkill Chemical Co.; Charles Dwyer, Standard Aromatics, Inc.; Gert Keller
and Henry Eickmeyer, Schimmel & Co., Inc.**



Nathan Frentz, Roubechez, Inc.; George Kolar, Kolar Laboratories, Inc.; and Stephen Goode, Rita Chemical Corp.



Ralph Messina, Colgate-Palmolive Co.; Samuel Cohen, Glyco Chemicals; and Kurt F. Neulinger, Croda, Inc.



E. Allen Newcomb, Malmstrom Chemical Corp.; W. C. Adrian, Chas. Pfizer & Co., Inc.

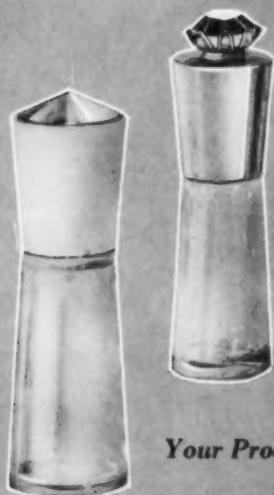
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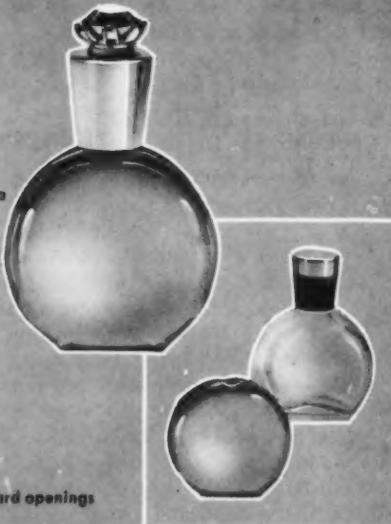
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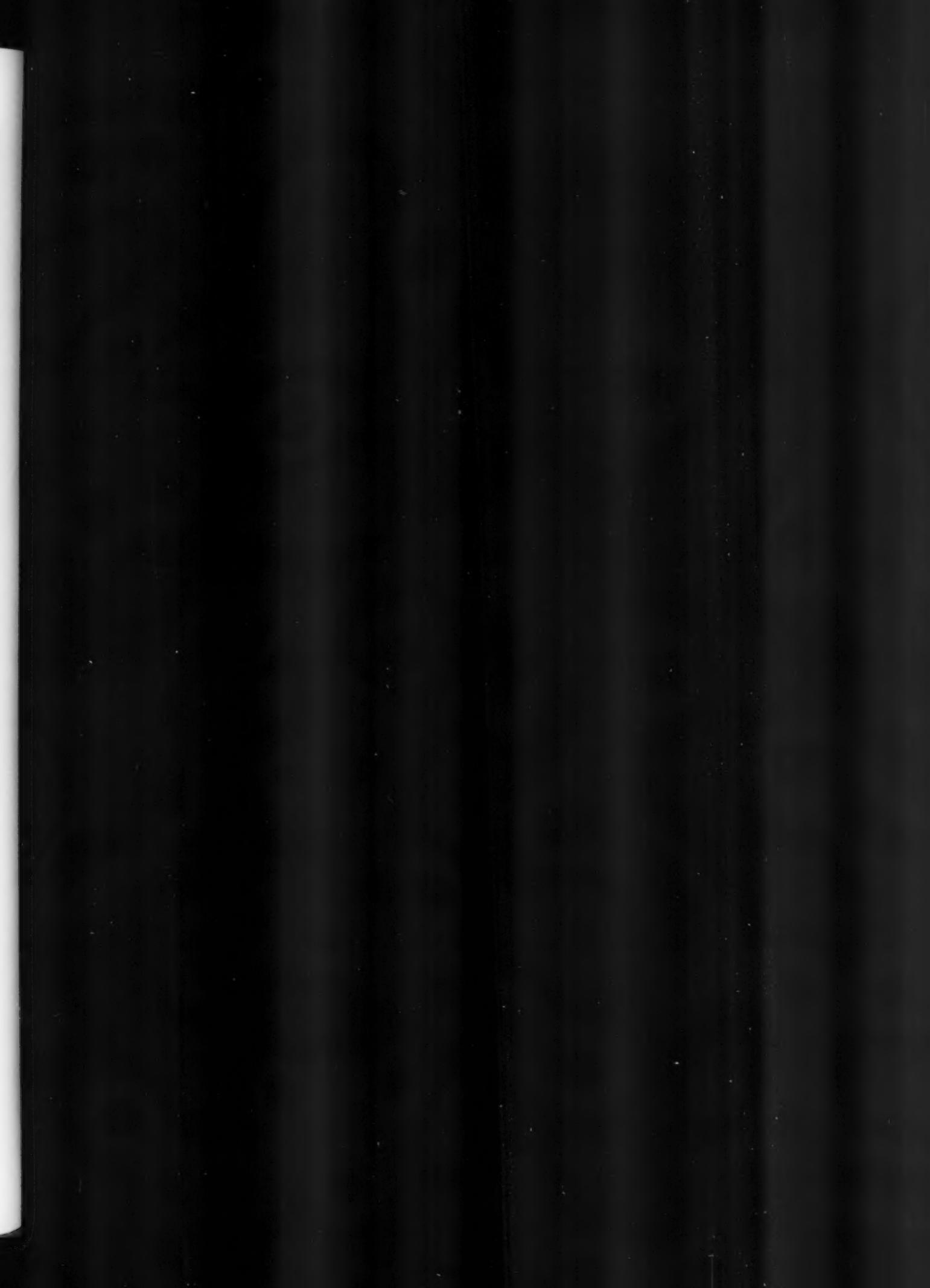
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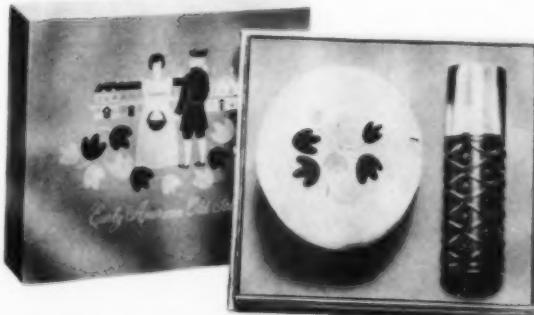
PACKAGING & PROMOTION



Lentheric has just added Bain d'Or Bath Soap to its line. The product is lightly scented with citrus notes of orange, lemon and bergamot, typical of the line. The soap contains skin softening emollients. Each bar carries the signature and is individually wrapped and sealed. Packaged three to a long, slender, marbleized box, tradition with the Bain d'Or line.



All-plastic container for deodorant has been adopted by Five Day Laboratories, division of Associated Products, Inc., New York. Cap and barrel have vertical grooves for appearance and grip. Push-up bottom is polyethylene. Container is made by Owens-Illinois Glass Co., Toledo, Ohio. Labels printed by National Label Co., Philadelphia.



Shulton's new package for Early American Old Spice line of women's toiletries was re-designed by firm's Packaging Art Director Gene DiScala. Package is vibrant blue for sheer impact at point of sale. Early American character of the original design and Spencerian script were maintained for product identification.



Stanley Home Products, Inc., Westfield, Mass. has bowed Lady Catherine spray cologne in glass-pressure bottle. It is sheathed in white plastic and topped with gold metal slip-on cap. Folding carton matches the bottle. Decorations designed by Margery Markley. Bottles by Owens-Illinois Glass Company, Toledo, Ohio; slip-on caps by Virjune Mfg. Co., Inc., Waterbury, Conn.; and cartons by Warner Brothers Co., Bridgeport, Conn.

Rosine Products, Inc., New York City is introducing nationally Glamour De Rose beauty and bath soap. It is deeply carved and resembles a rose. They are packed three to a box, which is gold and white, and of the clear-view type. The soap comes in pink, yellow, violet and blue.



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NEWS & EVENTS

New Sorbitol plant for Baird Chemical

Baird Chemical Industries, New York City, will build a \$1,500,000 plant on a 40-acre site near Peoria, Ill. for the production of Sorbitol. The plant will have a capacity of 20 million lbs.

Pope gets Fritzsche post

Lonnie H. Pope has been appointed sales representative in the newly established Dallas, Texas area of Fritzsche Brothers, Inc. Pope has been an analytical chemist for the New York City producer of essential oils, aromatic chemicals, and fragrance and flavor composition.

Digest of expiring pharmaceutical patents

A digest of expiring patents—pharmaceuticals is being published monthly, and contains summaries of the contents of pharmaceutical patents expiring during the same month one year later. Subjects covered include cosmetics, fine organic chemicals, essential oils, soaps, pharmaceuticals, patent medicines, chemotherapeutic agents, natural biological products, germicides, veterinary and nutritional products. Products and processes are described. The publisher is Louis Leaman, 26 Columbia St., Brookline 46, Mass.

Papers announced for TGA scientific section meeting Nov. 29

Four papers will be presented at the morning session of the scientific section meeting of the Toilet Goods Association which will convene Nov. 29 in the Empire Room, Waldorf-Astoria Hotel, New York City. They are:

Properties and Reactions of Hair after Treatment with Mercaptans and Differing Sulphydryl Acidities by J. W. Haefele and R. W. Broge, Procter & Gamble Co.

Response of Normal and Damaged Human Skin to Prolonged Topical

Treatment with Female Hormones by Herbert J. Spoor, Ph.D. and M.D., Cornell University College of Medicine.

Use of Water Soluble Certified Dyes in Oily Media by Robert L. Goldemberg, Shelia O'Leary and Nathan A. Ziskin, Shulton, Inc.

The Determination of Bacteriostats in Cosmetics: para hydroxy benzoate, dichlorophenol, hexachlorophene by P. D. Derry, M. Holden and S. H. Newburger, division of Color and Cosmetics, Food and Drug Administration, Department of Health, Education and Welfare.

Color additives is on the agenda for the afternoon session. This subject will be covered by a panel of experts, who will also answer questions from the floor and from members who submit them to the association in advance. Headquarters of the association are at 1270 Avenue of the Americas, New York City 20.

Allied Chemical gets new technical service lab

The technical service laboratory of Allied Chemical's General Chemical division has moved from Edgewater, N. J., to new quarters at the firm's Morris Township, N. J. research center. The new technical service facilities occupy part of a recently completed laboratory wing.

Lowenstein forms a cosmetic affiliate

Lowenstein Dyes and Cosmetics, Inc., is a newly-formed affiliate of Jos. H. Lowenstein & Sons, Inc., Brooklyn, N. Y. for dressing and dye supplier since 1897. The plant and laboratory is expected to be in operation by Sept. 15, and is located on the floor above the parent company.

Keenan named head of Philadelphia Pharmacy School

Dr. Vincent J. Keenan has been elected president of the Philadelphia College of Pharmacy and Science, succeeding the late Dr. Ivor Griffith.

Jones gets latest Fritzsche award

Professor E. R. H. Jones, Oxford England, was selected by the American Chemical Society, at the recent Chicago meeting, to receive the 1962 Fritzsche Award. Professor Jones has been cited for his outstanding contributions in the field of terpenoid chemistry, particularly the chemistry of the higher terpenes and the synthesis of terpenoids related to Vitamin A. His work has been authoritatively termed a "classical breakthrough in terpene chemistry, which has proved to be of enormous structural as well as biogenetic significance."

The award, a gold medal and cash prize, will be presented by a representative of Fritzsche Brothers, at the Spring meeting of the American Chemical Society.

Gunn re-elected head of DCATA

Philip A. Gunn, Dick Dunn Drug Products Company, has been re-elected president of the Drug-Chemical and Allied Trades Association of St. Louis.

Others re-elected to serve with Gunn are: First Vice President Norman A. Dietz, Julius Blackman Corp.; Second Vice President Norman E. Mendenhall; and Secretary-Treasurer William J. McMillan, Waddel & Reed.

New Board members include: Edward H. Baltzer, Fred A. Blust, McMillan, Mendenhall, Avon L. Michel and Charles H. Sweeney.—*Ted Young*, Director of Publicity DCATA.

Fritzsche expands in Chicago area

Fritzsche Brothers, Inc., New York City producer of essential oils, aromatic chemicals, flavor and fragrance compositions has added two new sales representatives in the Chicago Area. Russel E. Bull and Everett H. Johnson, Jr. are the new men named to aid veteran salesman Carl Edwards.

Johnson previously was with Polak's Frutal Works, and Bull has been with Fritzsche for some 14 years in the St. Louis area.

New Products

Aleuritic acid available in production quantities

Aleuritic acid, heretofore available only in experimental quantities, is now being produced commercially and at a quantity price.

Suggested use is in perfumery (Civetone, Dihydrocivetone and Epi-Ambrettolide) and pharmaceuticals, among others.

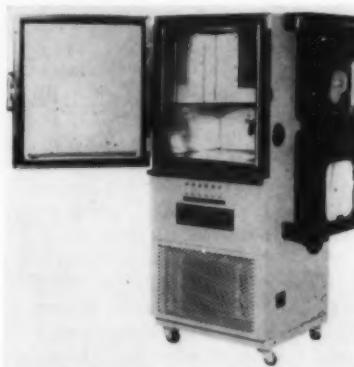
Aleuritic acid is extracted from shellac. Because of the position of its reactive hydroxyl and carboxyl groups, it serves as a versatile chemical intermediate in the synthesis of a number of chemicals.

Chemical properties are: Purity > 98%; Water < 0.4%; Melting Point 97-99°C; Acid Value, 181-185; Specific Gravity @ 20°C, 1.114; Approximate Weight, 4 lbs./gal.; Ash, Nil; Odor, Almost odorless; appearance, slightly yellow.

Pure aleuritic acid, available in limited quantities, can be obtained by the recrystallization of the technical

grade. It has a melting point of 101°C, and acid value of 184.3.

William Zinsser & Co., Dept. AP, 518 West 59th St., New York 19, N.Y.



Cabinet for temperature-environment testing

New unit provides test space of 5.1 cu. ft. in compact cabinet. The Tenney-Mite TH, Model TMTHO200

provides temperatures from 0° to +200°F, and relative humidity from 20% to 95% in the dry bulb range, limited by +35° to +185° dew point.

It can pull-down from +70° to 0°F in approximately $\frac{3}{4}$ hour. It heats from +70° to +200°F in approximately one hour. Work space has heli-arc welded stainless steel liner and is 21" x 25" x 17". The exterior is 26" x 62" x 33". Unit can be mounted on casters and requires no auxiliary equipment. Optional accessories include: window, light, windshield wiper, terminals and ports, and instrumentation is available as required.

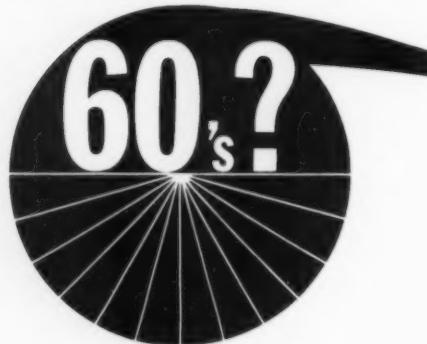
Tenney Engineering, Inc., Dept. AP, 1090 Springfield Road, Union, N.J.

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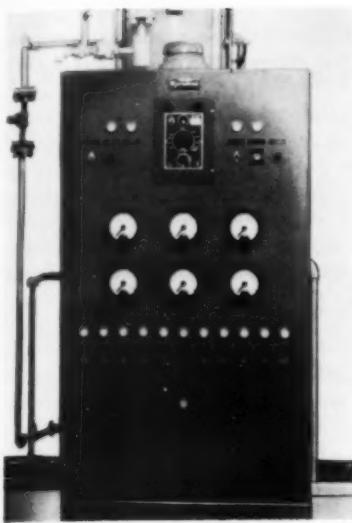
Helpful hints contained in Catalog 58-P

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and rinsing of the resin beds. After regeneration, the equipment returns to service automatically. Each step in the regeneration process can be adjusted individually to meet specific conditions and all valves have optional manual operation.

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verted to waste until the condition has been corrected. A full tank of demineralized water is maintained automatically.

Barnstead Still and Sterilizer Company, Dept. AP, 173 Lanesville Terrace, Boston 31, Mass.

Develop anti-perspirant aerosol package closure

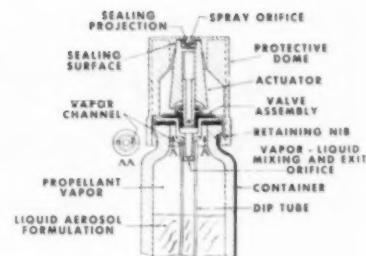
With the development of a non-metallic valve and a self-sealing cap, packaging of anti-perspirants in aerosol containers is now possible.

Heretofore, whenever an anti-perspirant has been tried in an aerosol package, the aluminum salts in the product have crystallized and clogged the valve.

Heart of the new development is not only the non-metallic valve but also the "corking" action of the self-sealing cap. This action minimizes clogging, between uses, caused by drying of the aluminum salts.

The "Vapor Mix" valve and "Seal Dome" closure have been designed for use with all containers (glass, aluminum, stainless steel, plastic) having openings 20mm or 1" diameter. Metal containers for aluminum salt-based formulations have to be protected against corrosion.

The interior of the cap (see drawing) is tapered to seal against the



sides of the vertical toggle-type "Micro-Mist" mechanical breakup actuator. Also it has a projection at the top which fits into the terminal orifice of the actuator, sealing it from the air. Ribs along the inner sides of the cap create a snap fit and cause it to grip the valve cup.

The valve has two small channels on either side of the nylon valve cup that fits into the dip tube. These channels allow a minute supplementary amount of propellant to enter the dip tube at the top. When the actuator is pressed, this added propellant, in vapor form, mixes with the liquified solution of product and propellant that is forced up through the dip tube in the normal way. This results in an unusually fine spray.

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News of the Societies

German Cosmetic Chemists meet

The Association of German Cosmetic Chemists will meet in the Winterhuder Fährhaus in Hamburg, October 25, at 8:00 p.m., following dinner. The meeting date does not interfere with other events of the DGF Jubilee Convention which may be of interest to the members of GKC.—by Dr. Herbert Neugebauer, Secretary, AGCC

SCC will cite Reed for helping industry

Raymond E. Reed, vice president in charge of technical operations of the Toni Company, has been chosen by the Society of Cosmetic Chemists to receive its 1961 Medal Award. He is being honored for his contributions to the birth and growth of the Society; for his many inventions, and particularly for the 18 patents relating to hair waving; for his understanding of the cosmetic chemist's relationship with management; and for the development of a research organization in his own company along the most mutually valuable and ethical lines.

Society President Dr. Sophie L. Plechner will pre-

sent the award at the Society's annual meeting on November 28, Hotel Biltmore, New York City. Dr. Milton Harris, vice president and director of research at Gillette, will be the eulogist.

Reed is generally considered to have done more to bring science into the cosmetic industry than any other man. As vice president in charge of technical operations for the Toni Company for the past 15 years, he has dedicated himself and inspired his associates to the development and merchandising of products that meet high performance, quality and ethical standards. Reed was at least 20 years ahead of his time in applying modern scientific techniques (similar to those originating in the pharmaceutical field) to the development of cosmetic products.

N.Y. Chapter SCC will honor president

Members of the New York Chapter of the Society of Cosmetic Chemists will honor SCC President Dr. Sophie Plechner at the monthly meeting Nov. 1, at the George Washington Hotel, Lexington Ave. at 23 St., New York City. This is the annual Presidents' Night.

A technical paper will be presented by Bernard H. Nappen, Application Research Group, National Starch Products Company. He will discuss the newer modifications of starches and the application of the new starch derivatives in cosmetic products.

The reception begins at 5:30 pm, and dinner and the technical paper follow.—by R. K. Lehne, Publicity Chairman, N. Y. Chapter SCC.

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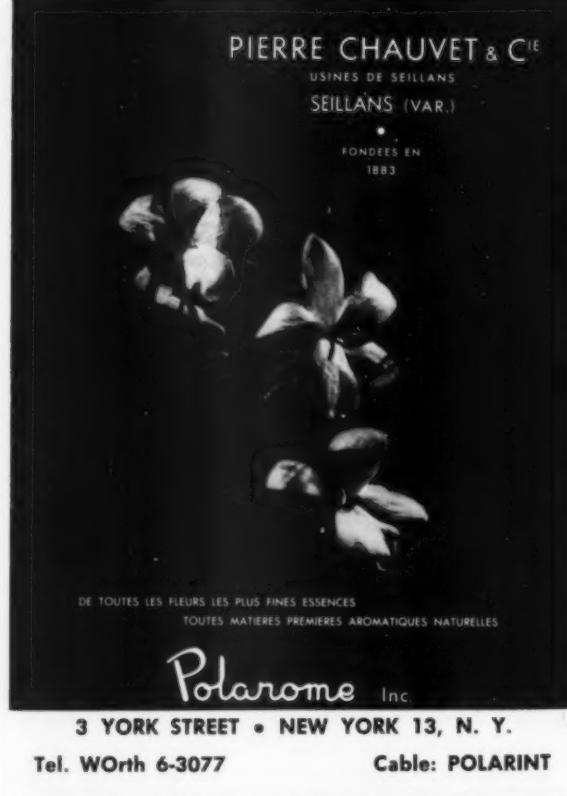


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INDUSTRY EVENTS CALENDAR

Oct. 15-20—4th International Congress of Allergology, Commodore Hotel, New York City.

Oct. 18—The American Society of Perfumers, Advertising Club, New York City.

Oct. 18-20—23rd Annual National Packaging Forum, Biltmore Hotel, New York City.

Oct. 31-Nov. 1—First International Symposium of Automatic Merchandising, McCormick Place, Chicago.

Oct. 31, Nov. 1-2—10th Canadian National Packaging Exposition, Automotive Bldg., Exhibition Park, Toronto.

Nov. 7-10—Packaging Machinery Manufacturers Institute Conference-Workshop and Exposition, Cobo Hall, Detroit, Mich.

Nov. 8—Committee on Cosmetics, American Medical Association, Symposium on Cosmetic Problems in General Practice, Dallas Memorial Auditorium, Dallas, Texas (2:00 p.m.) See abstracts page 36, this issue.

Nov. 14—Chicago Perfumery, Soap and Extract Assoc., Inc., Annual Thanksgiving Stag Party, Furniture Club of America, Chicago.



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Nov. 15—The American Society of Perfumers, Advertising Club, New York City.

Nov. 27-Dec. 1-28th Exposition of Chemical Industries, New York Coliseum, New York City.

Nov. 28—Society of Cosmetic Chemists, Annual Meeting, Hotel Biltmore, New York City.

Nov. 29—The Toilet Goods Association, Scientific Section Meeting, Empire Room, Waldorf-Astoria Hotel, New York City. (See page 57 for listing of papers that will be presented.)

December 12—Chicago Perfumery, Soap and Extract Association, Inc., Sheraton-Chicago Hotel, Chicago. Annual business meeting. (12:00 noon Luncheon)

Dec. 16—Chicago Perfumery, Soap and Extract Association, Inc., Grand Ballroom, Conrad Hilton Hotel Annual Christmas party. (Dinner-Dance).

1962

May 9—Scientific Section of the Toilet Goods Association, Inc., New York City. (Place to be announced later).

June 24-29—Joint Convention of the Toilet Goods Association, Inc. (USA) and the Toilet Goods Manufacturers' Association of Canada, Chateau Frontenac, Quebec, Canada.

July 2-5—The 2nd International Congress of Cosmetic Science, London, England.

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PERSONALITIES

Alfred S. Vassalo has been elected executive vice president of Fred Fear and Company, Brooklyn producer of flavoring extracts and food colors. Announced concurrently was the election of **Dr. Arthur S. Wendt** to vice president of the firm. Dr. Wendt has been technical director of the company for many years. He is vice pres-

ident of the Flavoring Extract Manufacturers Association and has served on the National Council of the Institute of Food Technologists.

Edouard Hache, director general of Firmenich et Cie., Paris, is currently visiting the United States. His headquarters are at the Firmenich offices in New York City. While in this country, Hache will visit many important American perfume and cosmetic firms, particularly those more directly associated with the French market.

Hache is widely recognized in the perfumery world as a creative perfumer and has served this profession his entire career.

Chemist Mrs. Amy Twanmoh has joined the organic research staff of Shulton, Inc., New York City. Prior to this appointment Mrs. Twanmoh was a chemist in the quality control laboratory of New York Quinine & Chemical Works.

John R. Torrens has been named vice president in charge of international operations at Andrew Jergens Co., Cincinnati. He will establish subsidiary operations abroad for Jergens and will supervise export sales. Torrens previously was vice president and general manager of Helene Curtis International, and formerly managed the Latin American division of Bristol-Myers International.

William B. Randall has been elected president of the Rolley Company, a division of Botany Industries, Inc., to succeed **Charles Rolley**, who has resigned. Randall was previously gen-

eral manager of the firm, maker of Sea & Ski sun tan lotion.

New manager of Kay Daumit (Lustre-Creme) sales in Colgate-Palmolive Company's Toilet Articles division is **Joseph J. Hirschberg**. He succeeds **Albert H. Endler**, new vice president and general manager of Reefer-Galler Incorporated, a newly-acquired Colgate-Palmolive subsidiary.

Nathan Ziskin has been appointed a cosmetic chemist at Shulton, Inc. He formerly was a research and development chemist for Yardley, and previously was with Revlon in a similar capacity.

Paul P. Woolard is newly elected president of Prince Matchabelli Inc., subsidiary of Chesebrough-Pond's Inc. **Jerome A. Straka**, corporation president, continues as chairman of the board and chief executive officer of the subsidiary.

As president of Prince Matchabelli, Woolard will be responsible for the Prince Matchabelli product line, Aziza eye cosmetics, Polyderm treatment products, Black Watch men's toiletries, and Simonetta perfume.

Woolard joined the firm as a salesman in 1950 and five years later was named general sales manager. He became vice president in charge of sales in 1957; vice president in charge of marketing in 1959; and executive vice president and a director of the subsidiary in December of last year.

Stephen G. Hoch is new director of the product application laboratory of Malmstrom Chemical Corp., Newark, N. J. and Brooklyn, N. Y. producer of lanolin and lanolin fractions. The firm is expanding its program to supply customers with specialized formulation service and technical advice on the use of lanolin. Hoch previously was with Revlon laboratories for the past four years.

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MISCELLANEOUS

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American Perfumer published monthly at Pontiac, Illinois for October, 1961.

1. The names and addresses of the publisher, editor, managing editor, and business managers are: Publisher, Mrs. Earl R. Allured, 418 N. Austin Blvd., Oak Park, Ill.; Editor, Stanley E. Allured, 418 N. Austin Blvd., Oak Park, Ill.; Managing editor, none; Business manager, James W. Allured, 418 N. Austin Blvd., Oak Park, Ill.

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3. The known bondholders, mortgagees, and other security holders owning or holding 1 percent or more of total amount of bonds, mortgages, or other securities are: None.

4. Paragraphs 2 and 3 include, in cases where the stockholder or security holder appears upon the books of the company as trustee or in any other fiduciary relation, the name of the person or corporation for whom such trustee is acting; also the statements in the two paragraphs show the affiant's full knowledge and belief as to the circumstances and conditions which stockholders and security holders who do not appear upon the books of the company as trustees, hold stock and securities in a capacity other than that of a bona fide owner.

5. The average number of copies of each issue of this publication sold or distributed, through the mails or otherwise, to paid subscribers during the 12 months preceding the date shown above was 2772.

JAMES ALLURED, Business Manager

Sworn to and subscribed before me this 19th day of September, 1961.
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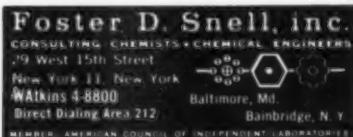
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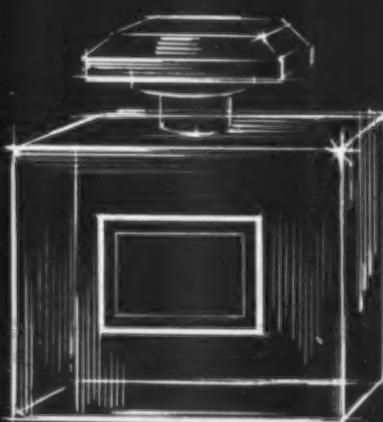
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